DEVOTED TO DISEASES
AND
PROCESSES OF
AGING

VOLUME 16 NUMBER 11
NOVEMBER 1961

Geriatrics

Radiation and Aging

Control of Chronic Pain

Combined Drug Therapy for Hypertension

Pathogenesis of Human Atheroarteriosclerosis

Prognosis and Treatment of Acromegaly

Complete table of contents on page 3A

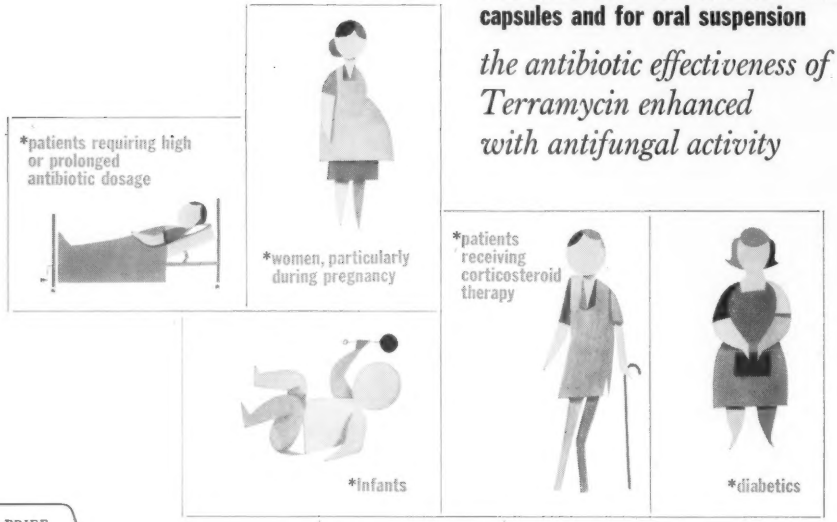
wherever
monilial superinfection
*is a particular hazard**

Terrastatin®

OXYTETRACYCLINE WITH GLUCOSAMINE PLUS NYSTATIN

capsules and for oral suspension

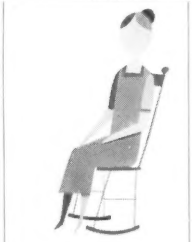
the antibiotic effectiveness of Terramycin enhanced with antifungal activity



IN BRIEF

Terrastatin (oxytetracycline with glucosamine and nystatin) provides the established antibiotic dependability of Terramycin® plus the potent antifungal activity of nystatin, which has a significant prophylactic action against intestinal monilial overgrowth.

INDICATIONS: Effective against both gram-positive and gram-negative bacteria, rickettsiae, spirochetes, large viruses, and certain parasites (amebae, pinworms), Terrastatin is indicated in a great variety of infections due to susceptible organisms, e.g., infections of the respiratory, gastrointestinal, and genitourinary tracts, surgical and soft-tissue infections, ophthalmic and otic infections, and many others. The added protection afforded by Terrastatin against monilial superinfection is especially important for those patients who are most likely to be susceptible to the overgrowth of *Candida albicans*.



ADMINISTRATION AND DOSAGE: Adults: Dosage providing 1 Gm. of oxytetracycline daily in four divided doses is usually effective. In *severe* infections, 2-4 Gm. daily may be indicated. Infants and children: 10-20 mg. of oxytetracycline per lb. of body weight daily.

SIDE EFFECTS AND PRECAUTIONS: If superimposed infection caused by resistant staphylococci is observed, the antibiotic should be discontinued, and a therapeutic trial of other antibiotics as indicated by susceptibility testing may be initiated. Aluminum hydroxide gel has been shown to decrease antibiotic absorption and is therefore contraindicated. Glossitis and allergic reactions are rare. Nystatin is virtually nontoxic and nonsensitizing; side effects are seldom observed. There are no known contraindications to glucosamine.

SUPPLIED: *Terrastatin Capsules*, 250 mg. of oxytetracycline with 250 mg. of glucosamine and 250,000 units of nystatin, bottles of 50. *Terrastatin for Oral Suspension*, each 5 cc. teaspoonful of reconstituted suspension contains 125 mg. of oxytetracycline with 125 mg. of glucosamine and 125,000 units of nystatin, 60 cc. bottles.

More detailed professional information available on request.

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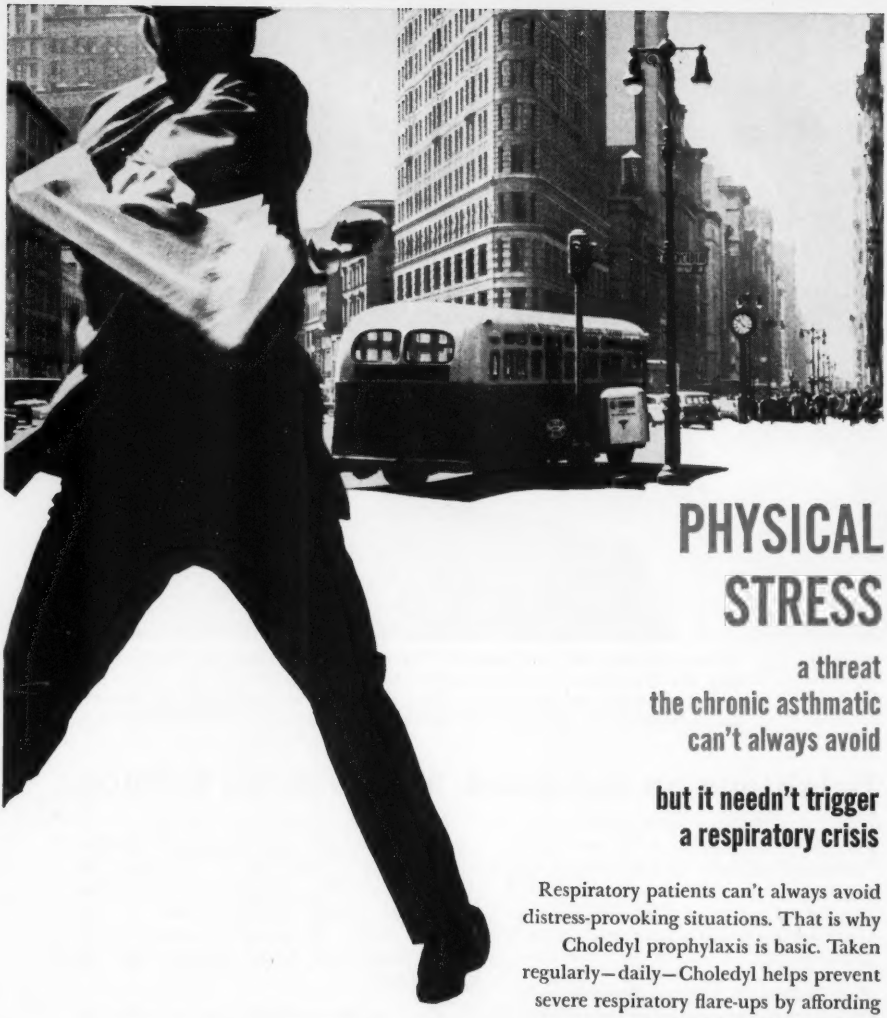

PHYSICAL STRESS

a threat the chronic asthmatic can't always avoid

but it needn't trigger a respiratory crisis

Respiratory patients can't always avoid distress-provoking situations. That is why Choledyl prophylaxis is basic. Taken regularly—daily—Choledyl helps prevent severe respiratory flare-ups by affording sustained bronchodilatation. Throughout long-term use, Choledyl is uniformly effective. And even in older patients, gastric upset and other unwanted effects are rare. *Dosage: one 200 mg. tablet q.i.d.*

Precautions: Side effects have been minimal but may include CNS stimulation or, rarely, palpitation. Full dosage information, available on request, should be consulted before initiating therapy.

to avoid the crisis in chronic bronchitis, chronic asthma, emphysema

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brand of oxtriphylline

GP14

THE CHOLINE SALT OF THEOPHYLLINE

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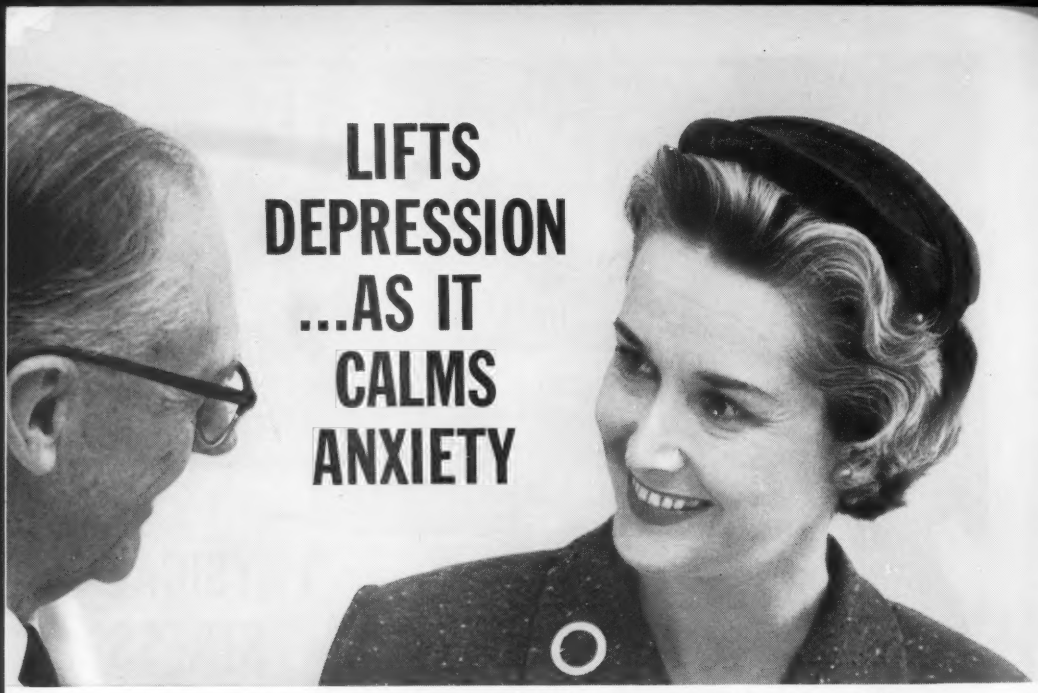

"I feel like my old self again!" Thanks to your balanced Deprol therapy, her depression has lifted and her mood has brightened up – while her anxiety and tension have been calmed down. She sleeps better, eats better, and normal drive and interest have replaced her emotional fatigue.

Brightens up the mood, brings down tension

Deprol's balanced action avoids "seesaw" effects of energizers and amphetamines. While energizers and amphetamines may stimulate the patient – *they often aggravate anxiety and tension.*

And although amphetamine-barbiturate combinations may counteract excessive stimulation – *they often deepen depression and emotional fatigue.*

These "seesaw" effects are avoided with Deprol. It lifts depression as it calms anxiety – a balanced action that brightens up the mood, brings down tension, and relieves insomnia, anorexia and emotional fatigue.

Acts rapidly – you see improvement in a few days. Unlike the delayed action of most other antidepressant drugs, which may take two to six weeks to bring results, Deprol relieves the patient quickly – *often within a few days.* Thus, the expense to the patient of long-term drug therapy can be avoided.

Acts safely – no danger of liver or blood damage. Deprol does not cause liver toxicity, anemia, hypotension, psychotic reactions or changes in sexual function – frequently reported with other drugs.

▲Deprol▲®

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this may be increased gradually up to 3 tablets q.i.d. With establishment of relief, the dose may be reduced gradually to maintenance levels.

Composition: 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

Supplied: Bottles of 50 light-pink, scored tablets. Write for literature and samples.

CD-5859

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Established 1946
Volume 16
Number 11

Geriatrics NOVEMBER 1961

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IN MINUTES...FOR HOURS...
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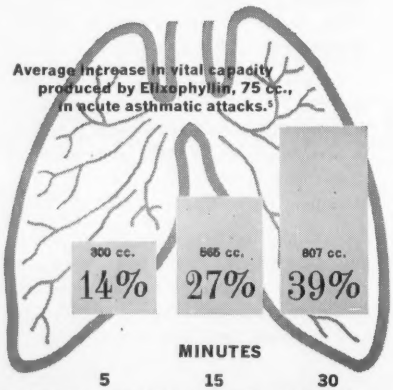

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New therapy for hypertension

Because of its action at the brainstem vasomotor control center, Capla is a new therapy for hypertension. It is effective alone in the treatment of mild to moderate hypertension, and can be combined with diuretics or peripherally acting antihypertensives in more severe cases.

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Controls blood pressure without serious side effects

Capla does not produce depression, postural hypotension, nasal congestion or gastric hyperacidity

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With Capla you have effective therapy without the unpleasant side effects which often cause patients to abandon treatment.

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Lowers blood pressure effectively in clinical use

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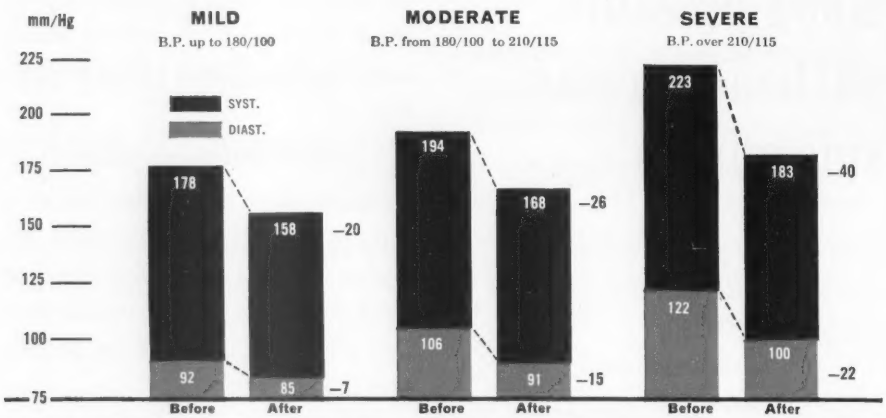
1. Berger, F. M., and Margolin, S.: A Centrally Acting Blood Pressure Lowering Agent (W-583). Fed. Proc. 20:113 (March) 1961. **2.** Diamond, S., and Schwartz, M. Scientific Exhibit at Ill. State Med. Soc. Chicago, (May) 1961. **3.** Douglas, J. F., Ludwig, B. J., Ginsberg, T. and Berger, F. M.: Studies on W-583 Metabolism. Fed. Proc. 20:113 (March) 1961. **4.** Duarte, C., Brest, A. N., Kodama, R., Naso, F., and Moyer, J. H.: Observations on the Antihypertensive Effectiveness of a New Propanediol Dicarbamate (W-583). Curr. Ther. Res., 2:148-52 (May) 1960 **5.** DuChez, J. W., Scientific Exhibit at Amer. Academy of Gen. Practice, Miami, (April) 1961. **6.** Kletzkin, M., and Berger, F. M.: A Centrally Acting Antipressor agent. Fed. Proc. 20:113 (March) 1961. **7.** Mulinos, M. G., Scientific Exhibit at Amer. Coll. Card. New York, (May) 1961 **8.** Mulinos, M. G., Saltefors, S., Boyd, L. J. and Cronk, G. A.: Human Pharmacology Studies with W-583. Fed. Proc. 20:113 (March) 1961. **9.** Shubin, H., Scientific Exhibit, Amer. Coll. Card. New York, (May) 1961.

Average Reductions In Systolic And Diastolic Blood Pressure Reported With Capla

(325 patients)



Usual dose, Capla 300 mg., q.i.d.—duration of therapy, 3 weeks to over 1 year.

These data show that Capla reduces both systolic and diastolic blood pressure, usually in proportion to initial pre-treatment elevations.

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SUPPLIED: bottles of 100, scored tablets.

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1. Griffith, R. S.: Antibiotic Med. & Clin. Therapy, 7:129, 1960.

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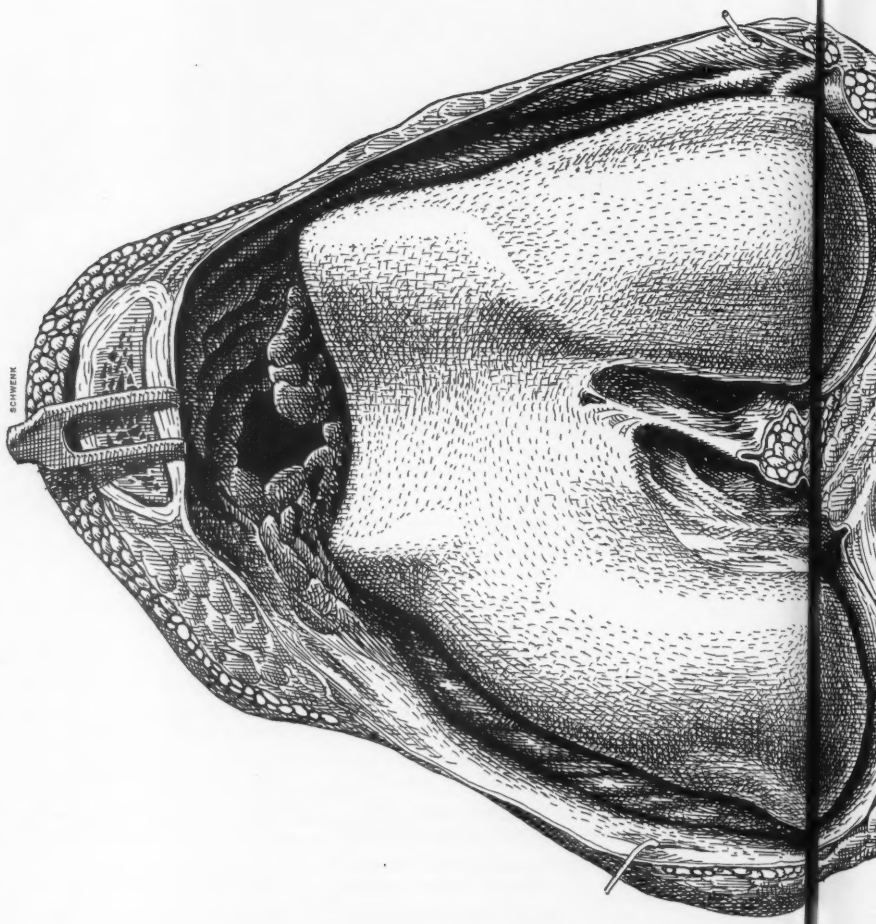

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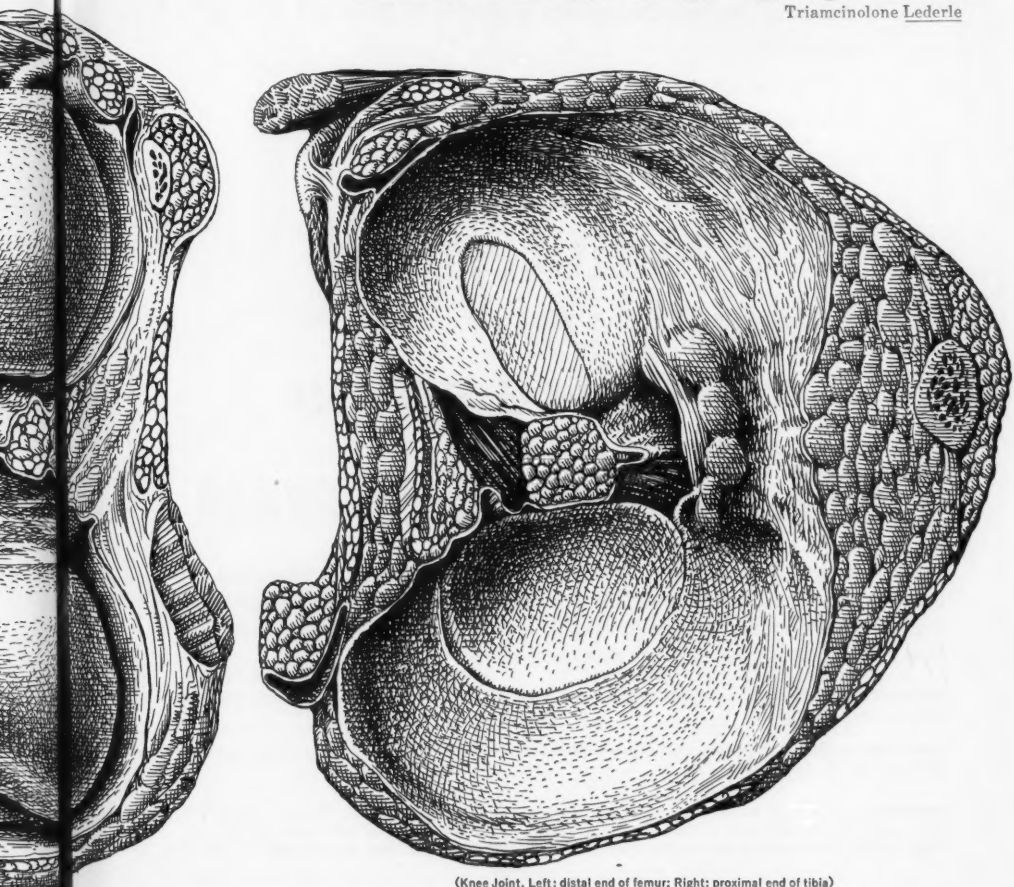

(Knee Joint, Left: distal end of femur; Right: proximal end of tibia)

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References (1) Moss, N. H.; Morrow, B. A.; Long, R. C., and Ravdin, I. S.: J.A.M.A. 140:1336, 1949. (2) Niemiro, B. J.: Journal-Lancet 71:364, 1951. (3) Combes, F. C.; Zuckerman, R., and Kern, A. B.: New York J. Med. 52:1025, 1952. (4) Lowry, K. F.: Postgrad. Med. 11:523, 1952. (5) Diamond, O. K.: New York J. Med. 59:1792, 1959.

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to prevent pain and anxiety in angina

For your angina patients, EQUANITRATE helps control pain and angina-triggering anxiety. EQUANITRATE reduces the number and severity of attacks, increases exercise tolerance, and lessens nitroglycerine dependence. Russek† reports "The best results . . . in both clinical and electrocardiographic response, were observed with a combination of meprobamate and pentaerythritol tetranitrate [EQUANITRATE] in the patients studied."

For further information on the limitations, administration, and prescribing of EQUANITRATE, see descriptive literature or current direction circular.

†Russek, H.I.: Am J. Cardiol. *3*:547 (April) 1959.

Supplied: EQUANITRATE 10 (200 mg. meprobamate, 10 mg. pentaerythritol tetranitrate), white oval tablets, vials of 50. EQUANITRATE 20 (200 mg. meprobamate, 20 mg. pentaerythritol tetranitrate), yellow oval tablets, vials of 50.

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Strain is a necessary component of man's efforts to move his external environment, but all too often brings on extreme pain and trauma when hard stools are moved after repair of rectal disorders. Metamucil adds soft, bland bulk to the bowel contents to stimulate normal peristalsis and also hold water within stools to keep them soft and easy to pass. Thus Metamucil, with an adequate water intake, is of great help in minimizing painful trauma to postsurgical rectal tissue. Metamucil promotes regularity through "smoothage" in all types of constipation.

brand of psyllium hydrophilic mucilloid

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Available as regular Metamucil or as the new lemon-flavored Instant Mix Metamucil

SEARLE

...In future issues

The December issue of *Geriatrics* will be devoted to the important subject, "The Old Person and His Social Environment." Included in the wide range of papers for this issue are the following:

▶ *Expectations for Older Persons in a Rural Community: Work and Retirement.* A study to determine the significance and meaning of retirement in a rural community was made by Joseph H. Britton, William G. Mather, and Alice K. Lansing, a research team from Pennsylvania State University. To collect the data, interviews were held with 487 adults of varying ages, living in or near a small Pennsylvania town. Health, finances, chronologic age, availability of jobs for younger workers, individual circumstances, and time remaining to enjoy life are factors to be considered with regard to retirement.

▶ *Social Adjustment of Spanish-American War Veterans.* Margaret R. Nichols and James F. Cummins of the Geriatric Clinic, Veterans Administration Outpatient Clinic, Boston, report on a study of social adjustment in a group of 85 alert, ambulatory, healthy, noninstitutionalized Spanish-American War Veterans. Of these 85, 61 per cent were still married, 76 per cent maintained their own dwellings, and 91 per cent were members of at least one social organization. The authors' research suggests (1) the close interdependence between prevention and therapy and between service and research with the older person, (2) the need for individualized services and technics, and (3) the value of reinforcement of the ego ideal and achievement and emphasis on continued growth, rather than on decline and continued aging.

▶ *Public Housing of Elderly in Chicago.* We have, in our urban centers, the picture of an aging population in quest of security and stability where imbalance and impermanence characterize many neighborhoods, write Bernard Kaplan, supervisor, community and tenant relations, Chicago Housing Authority, and William Hammond, assistant manager, Francis Cabrini Homes, Chicago. The authors discuss the three stages of the Authority's experience in sheltering the elderly: (1) housing without special planning and considerations; (2) special planning for occupancy and social services, but using facilities not especially designed for the elderly; and (3) integration of physical and social planning embodied in housing.

▶ *Another Approach to Nursing Home Care.* As the role of the nursing home in the community is beginning to be defined, the more progressive homes recognize their responsibility for providing enrichment programs as well as skilled nursing services and balanced diets, says Sidney Entman, executive director of the River Garden Hebrew Home for the Aged in Jacksonville, Florida. The administrator must always be conscious of the fact that his facility, no matter how good, is merely a substitute for the home life of the patient.

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ADVERTISING REPRESENTATIVES, NEW YORK 17: Bernard A Smiler, John Winter, George B. Janco, Ron Ziegler, 1 East 42nd Street. Telephone: Murray Hill 2-8717.
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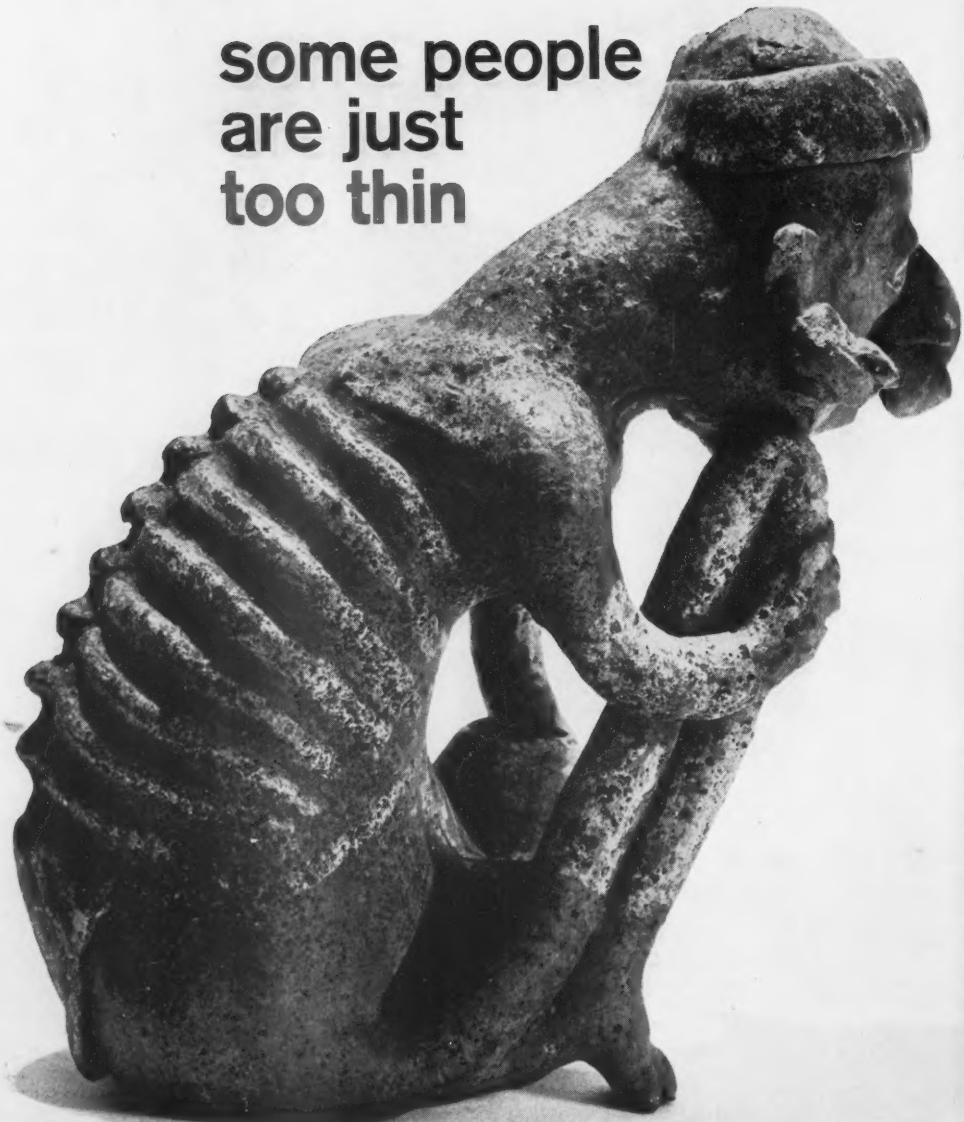
some people are just too thin



Effigies of pitifully emaciated people with ribs showing like "corrugated iron," such as this one from Nayarit, are typical of the tendency in primitive Western Mexican art to portray common illnesses and pathological deformations.

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adds working weight

Most underweight, debilitated patients show both objective and subjective improvement after anabolic therapy with Dianabol. In the chronically underweight patient, as well as in patients wasted and weakened as a result of aging, chronic or acute illness, trauma, or surgery, Dianabol promotes lean weight gain (averaging 5½ pounds and often exceeding 10 pounds) within several weeks. What's more, by improving weight status and general physical condition, Dianabol renews vigor and revives a sense of well-being in the patient who is **too thin.**

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*Misurale, F.: Minerva med. **51**:996 (March 21) 1960.

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Therapeutic guide

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Combining a superior skeletal muscle relaxant[1-3] with a preferred musculoskeletal analgesic,[4,5] *new* PARAFON FORTE rapidly relieves *both* pain and muscle stiffness in low back disorders. Thus, the effective dual action of PARAFON FORTE increases the patient's range of motion and hastens recovery. PARAFON FORTE is equally effective in other musculoskeletal disorders, such as myositis, whiplash injuries, strains or sprains, and fibrositis. Side effects are rare, almost never require discontinuation of therapy.

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PARAFLEX® Chlorzoxazone* 250 mg.
TYLENOL® Acetaminophen 300 mg.

Dosage: Two tablets q.i.d. *Supplied:* Scored, light green tablets, imprinted "McNEIL," bottles of 50.

References: (1) Settel, E.: Clin. Med. *6*:1373, 1959. (2) Peak, W. P. and Smith, R. T.: Penn. Med. J. *63*:833, 1960. (3) Mayle, F. C.; Sullivan, P. D., and Auth, T. L.: Med. Ann. D. C. *28*:499, 1959. (4) Roth, J. L. A.: Med. Clin. N. Amer. *41*:1517, 1957. (5) Batterman, R. C., and Grossman, A. J.: J.A.M.A. *159*:1619 (Dec. 24) 1955.

*U.S. Patent No. 2,895,877

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Digests from current literature

Digitalis in Surgery: Extension of Classical Indications

M. W. WHEAT, JR., and T. H. BURFORD. J. Thoracic. Surg. 41: 162-168, 1961.

Cardiac complications after major intrathoracic operations may be reduced from 20 to 10 per cent in patients over 55 years of age by prophylactic preoperative digitalization.

Patients under 60 years of age should be digitalized individually on the basis of estimated cardiac and pulmonary status and the magnitude of the operation. Postoperatively, patients are maintained on digitalis as long as indicated. Cardiac arrhythmias are easily controlled by increased digitalis or quinidine in patients who have received prophylactic digitalis.

Atrial fibrillation, atrial flutter, or congestive heart failure may occur postoperatively, particularly after pneumonectomy. Cardiac complications usually appear within one week and most often within seventy-two hours after operation. Withholding of digitalis until complications appear is no longer justified.

Preoperative electrocardiograms usually are not helpful in predicting the development of arrhythmias unless obvious changes occur. However, patients with previous cardiac disease, hypertension or asthma, or patients who have significant pulmonary emphysema or dyspnea upon exertion may be expected to have higher rates of cardiac complications.

A review of 439 patients, 55 years and older, who had had a major intrathoracic operation between 1948 and 1957, revealed that, of 302 who received no digitalis, 23 per cent developed cardiac complications; of 137 patients who received digitalis prophylactically, 12 per cent developed cardiac complications. The incidence of cardiac complications in patients over 70 years of age was 46.4 per cent without digitalization and only 10 per cent when prophylactic digitalis was given. Commonest complications were atrial fibrillation and flutter. Over-all mortality rate was 5 per cent in both groups.

Ulcerative Colitis in the Aged

Z. T. BERCOVITZ. Am. J. Gastroenterol. 35: 213-221, 1961.

The prognosis of ulcerative colitis in the aged is directly related to the age at onset: the older the patient, the poorer the prognosis. Secondary conditions, such as diabetes, arteriosclerotic heart disease, hypertension, arteriosclerosis, cardiovascular renal complications, and chronic liver disease, add to the seriousness of the colitis and hamper therapeutic efforts.

Treatment depends upon the presence of other conditions and the stage of the disease. Medical treatment includes whole blood transfusions, intravenous fluid replacement, electrolyte and protein replacement, and adrenocortical and antibiotic therapy. Diet also is important, the patient requiring more food than the average person because of loss of proteins and other valuable products. Vitamins are prescribed, and alcohol, coffee, and highly spiced foods are contraindicated.

Indications for surgery are massive or repeated hemorrhages, progressive decline of patient, intestinal obstruction, change from mild to fulminating disease with megacolon and impending perforation, and carcinoma. Hypothermia as an anesthetic adjunct reduces the possibility of shock and allows

(Continued on page 34A)

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A DISTINCT THERAPEUTIC ENTITY*
Restores and maintains skin's normal protective acidity—speeds natural healing and helps sensitive skin resist irritants and infection.

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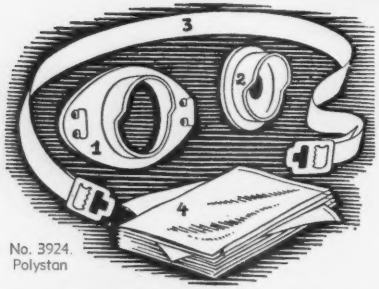

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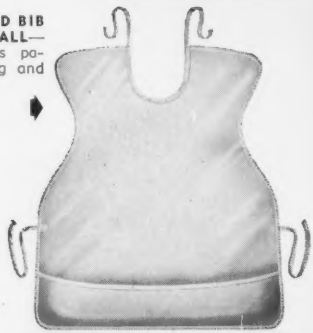

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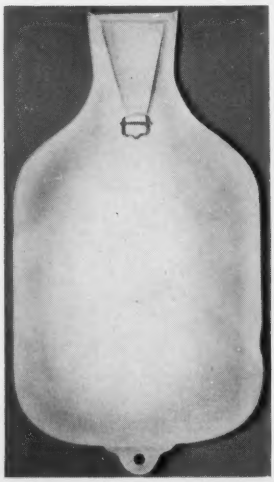

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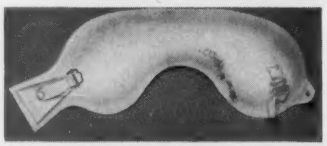

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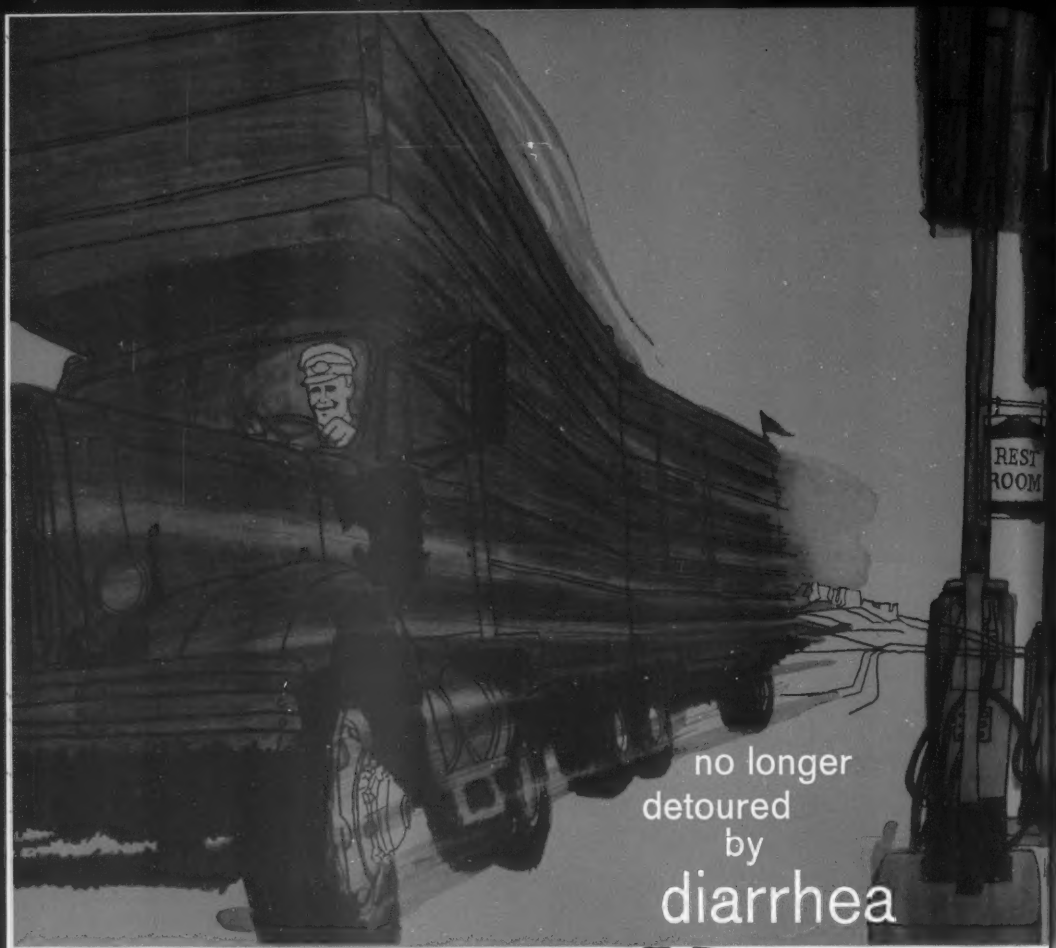

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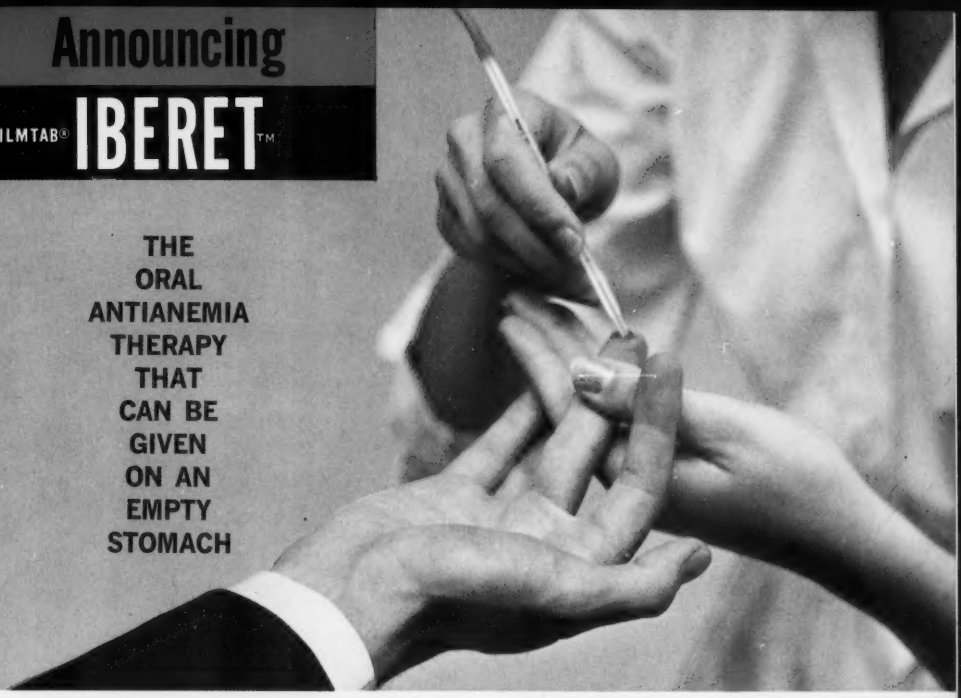

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Delivers 88% of its controlled release iron after the first half-hour
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The importance of the B-complex[2] and ascorbic acid to all cellular metabolic functions has been pointed out.[3] For this reason, therapeutic B-complex plus vitamin C are added to the Iberet formula to obtain maximal hematopoiesis in the shortest possible time.

In this half, 525 mg. of ferrous sulfate are provided in the ingenious Gradumet vehicle—engineered to deliver maximum release after the tablet is out of the stomach.

Here, to help insure maximal hematopoiesis, is therapeutic B-complex plus 150 mg. of vitamin C.

Just *one* Iberet Filmtab® a day supplies potent antianemia therapy—provides approximately the same hemoglobin response as ferrous sulfate given two or three times a day. Give Iberet at any time of day or night, even on an empty stomach. Iberet delivers most of its iron when and where it's best used—in the intestine.

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Plus Therapeutic B-Complex

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Thiamine Mononitrate	6 mg.
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Plus Vitamin C

Ascorbic Acid	150 mg.

Note: Filmtab® Fero-Gradumet™ with 105 mg. of Elemental Iron only, in long-release dose form, is also available.

[1] Woodruff, C.W., "Iron"; Borden's Review of Nutrition Research, 20:61, 1959.
[2] Vilter, R.W., "Essential Nutrients in the Management of Hematopoietic Disorders of Human Beings"; Am. J. Clin. Nutrition, 3-72, 1955.
[3] Brown, M.J., "Nutritional Problems in Surgery"; Surg. Clin. North America, 34-1239, 1954.

*In controlled-release dose form.
Filmtab—Film-sealed tablets, Abbott: U.S. Patent No. 2,881,085.
Iberet—Vitamin B-Complex, Vitamin C, and Controlled-Released Iron, Abbott.
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He's crossed a somewhat arbitrary point in life over into what's been dubbed "the geriatric years." In many ways, though, you'd never really know it. (Not to suggest that he'd *seriously* consider following the elusive current leading to Easter Island.)

But, he is nonetheless busy. He works . . . has hobbies . . . keeps up with the world around him.

And one way for you to help keep your geriatric's attitude optimistic, rather than diffident, is through Filmtab Gerilets. For, with Gerilets, you're prescribing dietary and therapeutic support which can contribute towards: improving functions illness or age have impaired—toning up the patient's appetite—brightening his overall outlook.

Dosage? Easy. Just a single, tiny pleasant-to-take Gerilets Filmtab a day.

ONE GERILETS FILMTAB PROVIDES:

B-Complex Vitamins
Thiamine Mononitrate (B_1) 5 mg.
Riboflavin (B_2) ..... 5 mg.
Pyridoxine Hydrochloride (B_6) ..... 1 mg.
Nicotinamide..... 20 mg.
Calcium Pantothenate..... 5 mg.

Oil Soluble Vitamins
Vitamin A.... 1.5 mg. (5000 units)
Vitamin D... 12.5 mcg. (500 units)
Vitamin E..... 10 Int. units

Hematopoietic Factors
Cobalamin (Vitamin B_{12})... 5 mcg.
Ferrous Sulfate, USP..... 75 mg.
(representing 15 mg. elemental iron)
*Folic Acid..... 0.25 mg.

Capillary Stability
Ascorbic Acid (C)..... 50 mg.
Quertine®..... 12.5 mg.
(Quercetin, Abbott)

Lipotropic Factors
Betaine Hydrochloride..... 50 mg.
Inositol..... 50 mg.

Anti-Depressant
Desoxyn®..... 1 mg.
(Methamphetamine Hydrochloride, Abbott)

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Sulestrex®..... 0.3 mg.
(Piperazine Estrone Sulfate, Abbott)
Methyltestosterone..... 2.5 mg.

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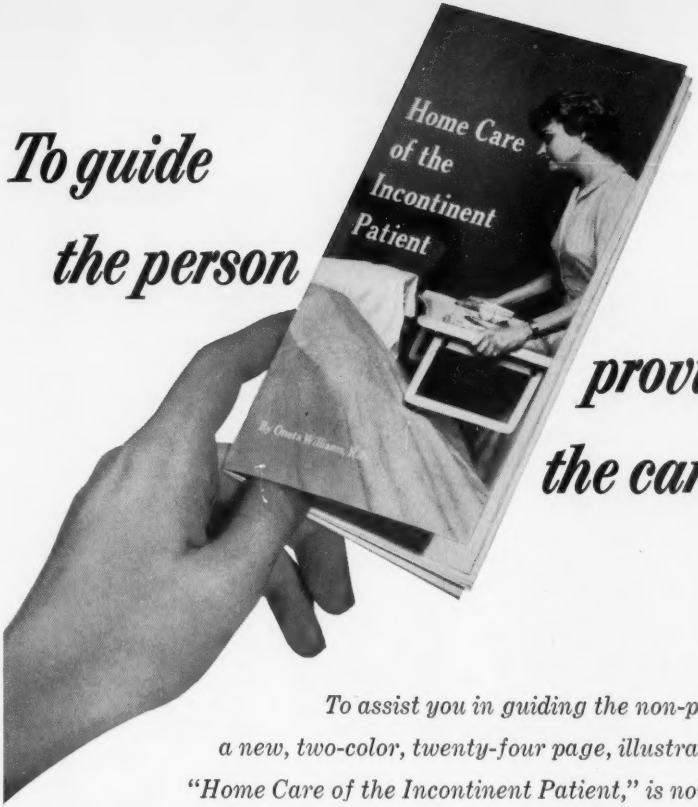
*FOLIC ACID DOES NOT CONTROL THE NEUROLOGICAL SYMPTOMS OF PERNICIOUS ANEMIA.

To guide the person providing the care...



To assist you in guiding the non-professional, a new, two-color, twenty-four page, illustrated booklet, "Home Care of the Incontinent Patient," is now available.

Written in non-technical language by a registered nurse, it outlines correct nursing procedures and discusses the psychological problems of caring for an incontinent at home.

Complimentary copies are available to you for distribution to your patients.

Write: Professional Products Division, Chicopee Mills, Inc.

These home nursing aids are available in drugstores everywhere.

Chux® Disposable Underpads
Controls fluid and fecal discharges while keeping bed linen clean and dry. Medicated to help prevent skin irritation. Available (13" x 17½" and 17½" x 24")

Chix® Adult Gauze Diapers
With extra absorbent center panel offering complete protection for both bedridden and ambulatory incontinents. Fits any waist size up to 44".

Chix® Cleaners
Soft, disposable, fabric tissue. Used wet or dry as an ointment applicator or rectal wipe.

PROFESSIONAL PRODUCTS DIVISION CHICOPEE MILLS, INC. 47 Worth Street, New York 13, N.Y.

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for more rapid and precise surgical technic.

Postoperatively, the blood values of calcium, proteins, and electrolytes are followed. Whole blood transfusions are given until hemoglobin, hematocrit, and blood pressure are stable. To prevent sudden peripheral vascular collapse, steroids should be administered, especially from the second to the seventh postoperative day.

Bile Peritonitis

I. COHN, JR., A. M. COTLAR, M. ATIK, W. M. LUMPKIN, T. L. HUDSON, and G. J. WERNETTE. Ann. Surg. 152: 827-835, 1960.

Antibiotic treatment significantly increases survival in experimental bile peritonitis in dogs regardless of route and time of administration, indicating that chemical peritonitis due to bile salt intoxication may not be isolated as the main or primary cause of a lethal outcome. Since dog bile is usually sterile, the antibiotics evidently act upon bile stimulated bacterial flora already within or accessible to the peritoneal cavity.

In the experiment, bile peritonitis was produced in unselected dogs by opening the fundus of the gallbladder and suturing the mucosa in eversion to allow continuous drainage of the animal's own bile into the peritoneal cavity. At the beginning of the operation, bile was aspirated from the gallbladder into a sterile syringe and at the end of the operation was injected into the peritoneal cavity. An initial insult of 1 cc. of bile per kilogram of body weight was found essential for uniform results. The dogs were divided into 6 groups: 1 control group, 4 groups receiving various forms of antibiotic therapy, and 1 group receiving gas gangrene antitoxin without antibiotics.

Animals in the control group received no treatment and had an average survival of about twenty hours; all died within thirty-seven hours. Cultures obtained from peritoneal cavities in 11 animals were positive for clostridia and staphylococci, except 1 which was positive for bacteroides.

Animals receiving preoperative bowel antisepsis with neomycin and tetracycline and intramuscular penicillin and tetracycline at the time of operation and four days postoperatively died or were killed from eight to twenty-three days after creation of their biliary fistula; 1 died at twenty hours. Peritoneal contents varied between 1,450 and 4,800 cc. of deeply bile-stained but not foul-smelling fluid. Cultures at death or sacrifice were negative in 2 experiments and positive only for yeasts in 1. Animals on less intensive antibiotic therapy had similar high survival rates. Even a single injection of antibiotic administered before operation was sufficient to completely alter the course of bile peritonitis. Dogs treated with antitoxin succumbed at about the same rate as untreated animals.

Combined Therapy of Inoperable Lung Carcinoma with 5-Fluorouracil and Irradiation

F. M. WILLETT, L. V. FOYE, JR., M. ROTH, and B. E. HALL. Dis. Chest 39: 38-41, 1961.

Simultaneous adminstration of low doses of x-ray and 5-fluorouracil appears to be beneficial in the treatment of inoperable epidermoid carcinoma of the lung. Whereas 5-fluorouracil alone is ineffective in pulmonary carcinoma, the compound may potentiate the antitumor effect of radiotherapy. Toxic manifestations of pharyngitis, esophagitis, leukopenia, and thrombocytopenia are transient and disappear within seven to ten days after cessation of therapy.

Irradiation is administered at 250 kv. in daily tumor doses of 100 to 200 r. five days a week to a total tumor dose of 2,000 r. The 5-fluorouracil is given intravenously over a two- to three-hour period in 200 to 500 cc. of normal saline, starting on the first day of x-ray therapy and continuing until such therapy is completed. The dose schedule for administration of 5-fluorouracil is as follows: on days 1 through 4, 15 mg. per kilogram of body weight, not to exceed 1,000 mg. per day; on day 5 and twice

(Continued on page 40A)

Take an "inside look" at a remarkable advance in topical steroid therapy

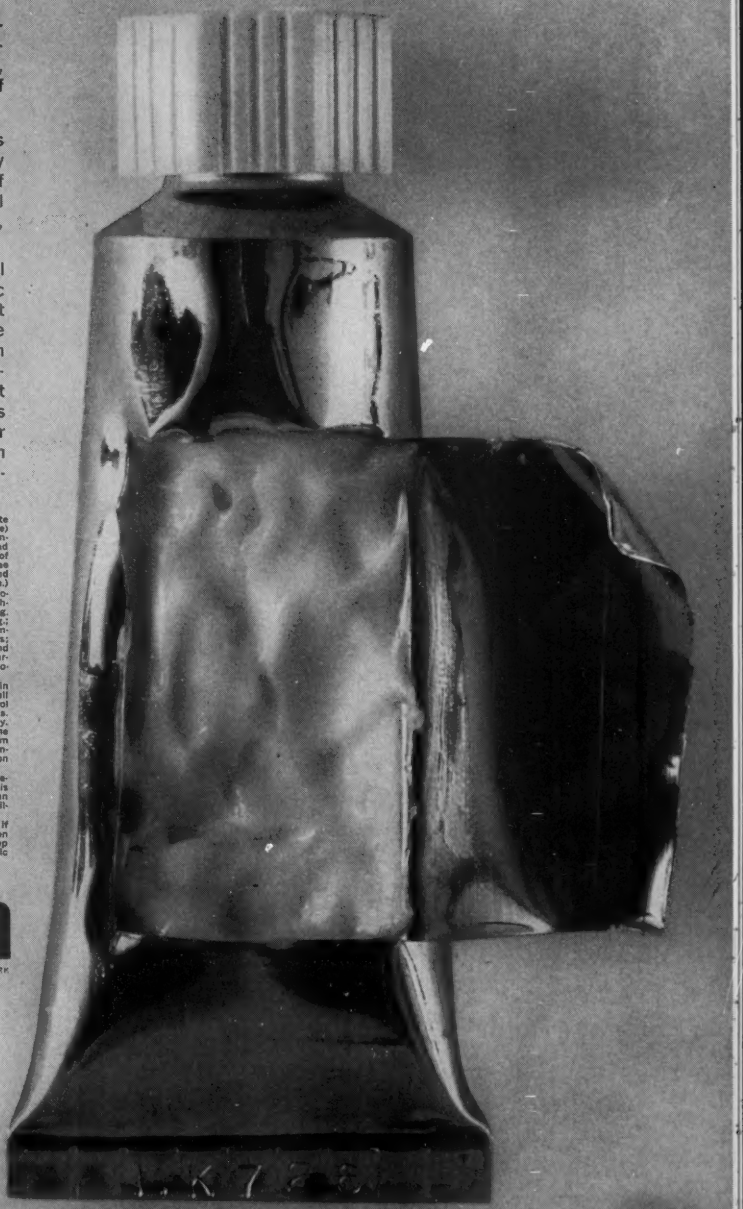
The unique base, Veriderm, combined with the outstanding anti-inflammatory steroid, Medrol, provides effective treatment of dermatoses.

Veriderm Medrol Acetate consists of Veriderm, a base closely approximating the composition of normal skin lipids, and Medrol Acetate, the highly effective, dependable corticoid.

Topical use of Veriderm Medrol Acetate produces symptomatic relief and objective improvement of dermatoses, and at the same time aids in correcting dry skin conditions. Veriderm Medrol Acetate, less greasy than an ointment and less drying than a lotion, is indicated in atopic, contact, or seborrheic dermatitis, and in neurodermatitis, anogenital pruritus, and allergic dermatoses.

Available in four formulations: Veriderm Medrol Acetate 0.25% — Each gram contains: Medrol (methylprednisolone) Acetate 2.5 mg.; Methylparaben 4 mg.; Butyl-p-hydroxybenzoate 3 mg.; in a skin lipid base composed of saturated and unsaturated free fatty acids; triglycerol and other esters of fatty acids; saturated and unsaturated hydrocarbons; free cholesterol; high-molecular-weight alcohol; with water and aromatics. (Veriderm Medrol Acetate 1% is also available.)
For prophylaxis against secondary infection: Veriderm Neo-Medrol Acetate 0.25% — Each gram contains: Medrol (methylprednisolone) Acetate 2.5 mg.; Neomycin Sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); Methylparaben 4 mg.; Butyl-p-hydroxybenzoate 3 mg.; in a skin lipid base composed of saturated and unsaturated free fatty acids; triglycerol and other esters of fatty acids; saturated and unsaturated hydrocarbons; free cholesterol; high-molecular-weight alcohol; with water and aromatics. (Veriderm Neo-Medrol Acetate 1% is also available.)
Administration: After careful cleansing of the affected skin to minimize the possibility of introducing infection, a small amount of either Veriderm Medrol Acetate or Neo-Medrol Acetate is applied and rubbed gently into the involved areas. Application should be made initially one to three times daily. Once control is achieved — usually within a few hours — the frequency of application should be reduced to the minimum necessary to avoid relapses. The 1% preparation is recommended for beginning treatment and the 0.25% preparation for maintenance therapy.
Contraindications: Local application of Veriderm Medrol Acetate or Neo-Medrol Acetate is contraindicated in tuberculosis of the skin and in other cutaneous infections for which an effective antibiotic or chemotherapeutic agent is not available for simultaneous application.
These preparations are usually well tolerated. However, if signs of irritation or sensitivity should develop, application should be discontinued. If bacterial infection should develop during the course of therapy, appropriate local or systemic antibiotic therapy should be instituted.
Supplied in 5 Gm. and 20 Gm. tubes.

Veriderm TRADEMARK
Medrol† Acetate
Neo-Medrol† Acetate



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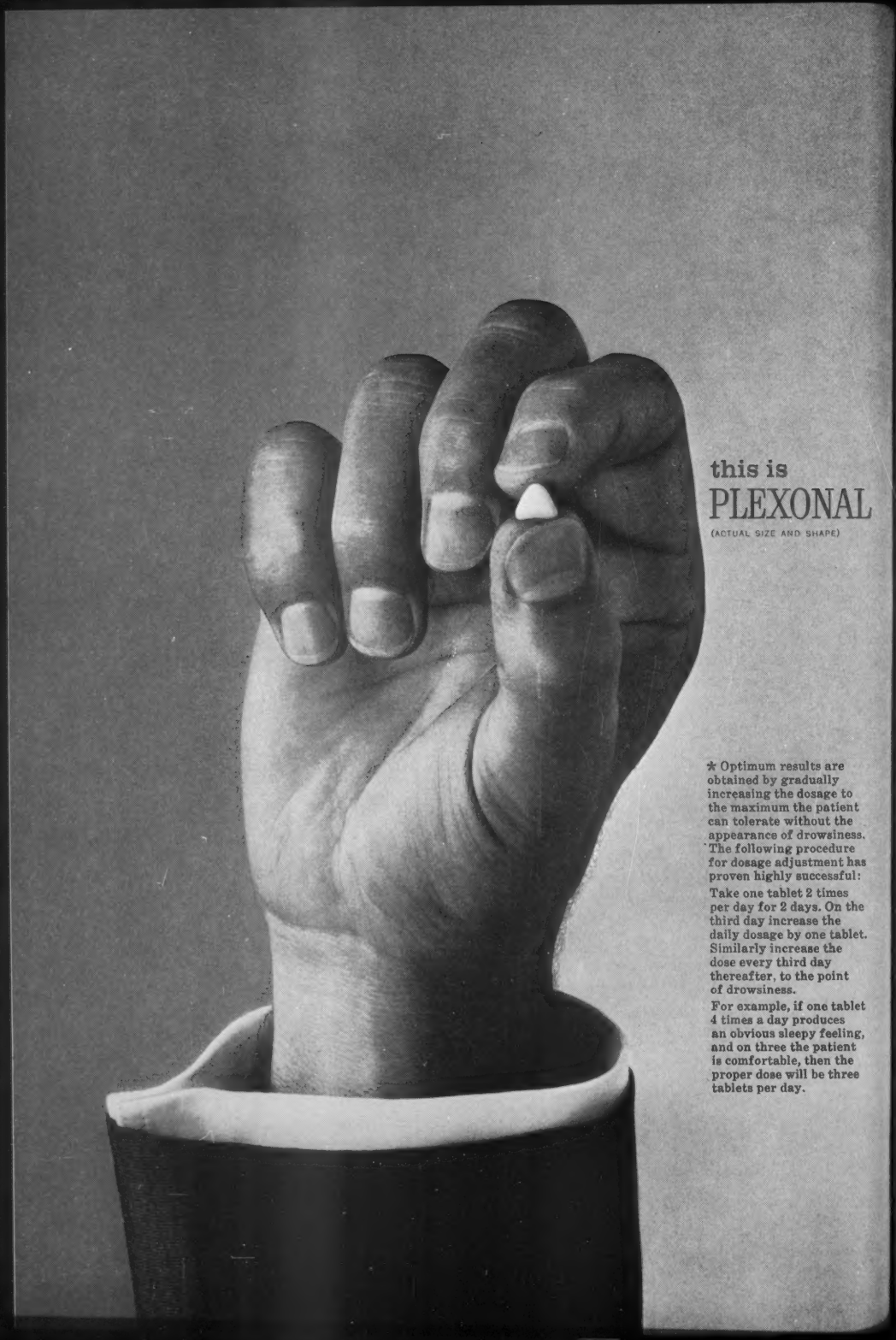

★ Optimum results are obtained by gradually increasing the dosage to the maximum the patient can tolerate without the appearance of drowsiness. The following procedure for dosage adjustment has proven highly successful:

Take one tablet 2 times per day for 2 days. On the third day increase the daily dosage by one tablet. Similarly increase the dose every third day thereafter, to the point of drowsiness.

For example, if one tablet 4 times a day produces an obvious sleepy feeling, and on three the patient is comfortable, then the proper dose will be three tablets per day.

a superior daytime relaxing agent

(NOT A TRANQUILIZER)

PLEXONAL®

Comparative clinical studies show that PLEXONAL is superior to meprobamate or barbiturates for daytime relaxation[1,2]

"Plexonal was preferred (superior therapeutic effect) by 73.7 per cent of the patients, whereas 11.1 per cent preferred meprobamate, a ratio of 6.6 to 1. . . . 30.5 per cent noted adverse reactions to meprobamate as compared to 7 per cent in respect to Plexonal. . . . Plexonal gave better results than did any of the sedative or relaxing agents that have been available during our experience covering the previous 15 years."[1]

In 26 older age cardiac patients, "A comparison of Plexonal with the therapy previously employed showed that 17 did better on Plexonal than on meprobamate, 6 did better on meprobamate than on Plexonal and 3 responded the same to both."[2]

Indications: Anxiety, tension, apprehension, nervousness, irritability, restlessness, hyperexcitability.

Extremely well tolerated by geriatric patients who need mild sedation, as well as by depressed patients.

Dosage: One tablet 3 or 4 times a day is adequate for most patients. However, some require up to six tablets per day, whereas others respond adequately to as little as 1 tablet per day.*

Composition: Each tablet contains sodium diethylbarbiturate 45 mg., sodium phenylethylbarbiturate 15 mg., sodium isobutylallylbarbiturate 25 mg., scopolamine hydrobromide 0.08 mg., dihydroergotamine methanesulfonate 0.16 mg.

1. Scheifley, C. H.: Proc. Staff Meet. Mayo Clin. 34:408 (Aug. 19) 1959.
2. Davanloo, H.: Am. J. of Psychiat. 117:740 (Feb.) 1961.

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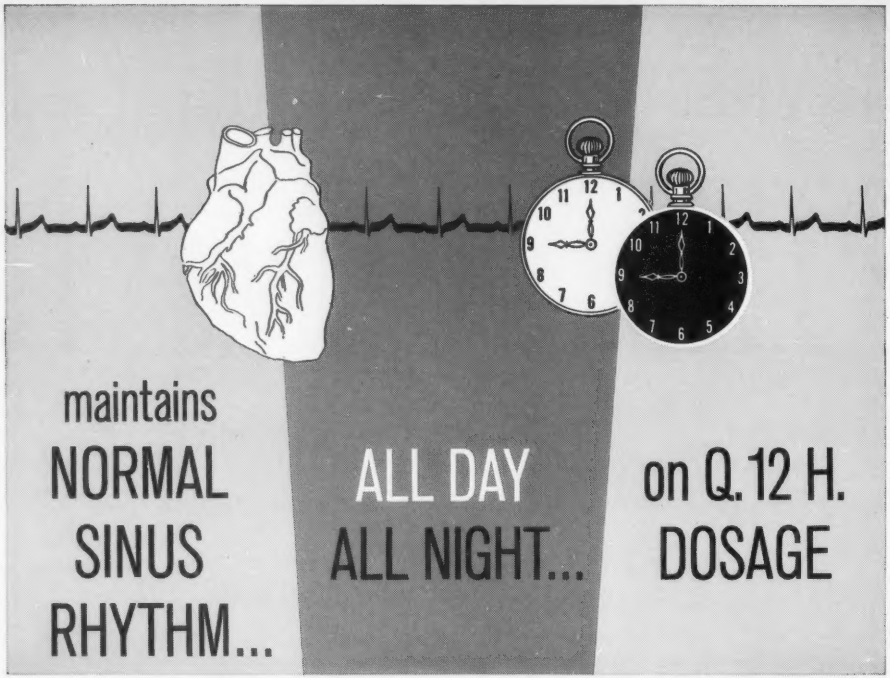

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DURA-TABS®

exclusive oral Sustained Medication*
Quinidine Gluconate 5 gr. (0.33 Gm.)

IN CARDIAC ARRHYTHMIAS[1-10]

Maximum efficacy: maintains effective quinidine blood levels all day, all night. **Better tolerated:** because quinidine gluconate is 10 times as soluble as the sulfate, and only part of daily Dura-Tab dosage contacts gastric mucosa. **Maximum convenience:** given q. 12 h.—no night dosage needed.

DOSAGE: for conversion of auricular fibrillation to normal sinus rhythm, in most cases, 2 Dura-Tabs 3 or 4 times a day, for 2 to 3 days; longer periods are required in some patients. **For maintenance,** 2 Dura-Tabs q. 12 h. in most patients... Bottles of 30, 100 and 250 Quinaglute Dura-Tabs.

For SAMPLES and complete literature[1-10] giving indications, cautions, etc., write

REFER TO PDR Page 821

WYNN PHARMACAL CORPORATION
Lancaster Ave. at 51st St., Philadelphia, Pa.

*U.S. Patent 2,895,881

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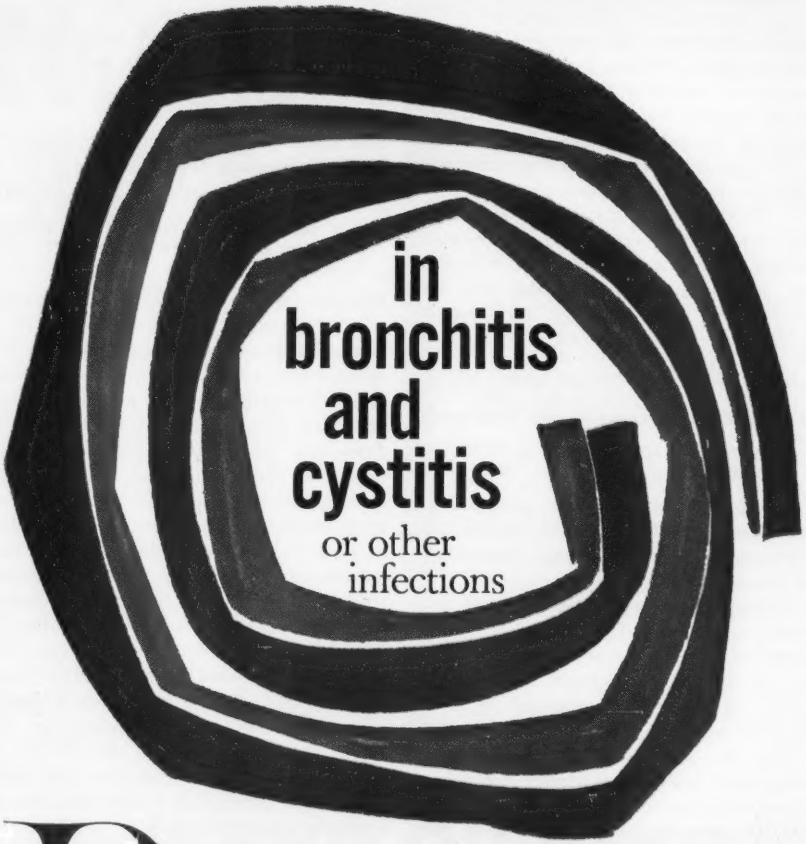

antibiotic therapy with an added measure of protection

DECLOMYCIN®

DEMETHYLCHLORTETRACYCLINE LEDERLE

against relapse—up to 6 days' activity on 4 days' dosage
against secondary infection—sustained high activity levels
against "problem" pathogens—positive broad-spectrum antibiosis

CAPSULES, 150 mg., 75 mg.; PEDIATRIC DROPS, 60 mg./cc.; SYRUP, 75 mg./5 cc.

Request complete information on indications, dosage, precautions and contraindications from your Lederle representative or write to Medical Advisory Department.

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

weekly thereafter, 7.5 mg. per kilogram, not to exceed 500 mg. per day. The usual course of combined therapy requires two weeks during which the patient receives about 90 mg. per kilogram of 5-fluorouracil.

Of 16 patients with inoperable epidermoid lung carcinoma treated with combined x-ray and 5-fluorouracil therapy, all had notable and rapid regression of the tumor mass. Several patients were alive and comfortable six months after therapy, and one was ambulatory and symptom free twelve months after therapy. Toxicity occurred in 11 of 16 patients.

Thrombosis: Prevention and Treatment

H. L. DEATON, W. G. ANLYAN, D. SILVER, and J. WEBSTER. Surgery 49: 130-141, 1961.

Plasmin therapy prevents postoperative thrombosis and dissolves fresh arterial clots without producing significant hemorrhage or hematoma formation.

Objective evidence of clot removal, consisting of a return of absent pulses, arteriograms or venograms showing the open vessel, or retinal photographs revealing restored circulation, was observed in 15 of 23 plasmin-treated patients.

The only changes as revealed by blood coagulation studies after fibrinolysin therapy were the fibrinogen level and the euglobulin clot lysis time. Prolonged prothrombin times were noted with higher doses of plasmin. Side effects of therapy were minor and consisted of a febrile response in 4 patients and transient arthralgia twenty-four hours after discontinuation of therapy in another.

A right femoral arterial thrombosis occurred in 1 patient after pelvic perfusion with chemotherapeutic agents for ovarian intra-abdominal carcinomatosis. The artery was reopened on 3 occasions to evacuate a fresh thrombus. Immediately after operation, the femoral and distal arterial pulses disappeared and the leg became cool and white. Plasmin therapy was started three hours later. Within twenty-four hours, the femoral and distal pulses, with the exception of the dorsalis pedis pulse, had returned and the limb was warm and pink. There was no evidence of hematoma formation or bleeding from the multiple surgical incisions.

The Direct Effects of Norepinephrine, Epinephrine, and Methoxamine on Myocardial Contractile Force in Man

L. I. GOLDBERG, R. D. BLOODWELL, E. BRAUNWALD, and A. G. MORROW. Circulation 22: 1125-1132, 1960.

Norepinephrine, epinephrine, mephentermine (Wyamine), and metaraminol (Aramine Bitartrate) substantially increase myocardial contractile force in man. Methoxamine (Vasoxyl), however, has virtually no effect on myocardial contractile force in doses that produce pronounced increases in arterial pressure. Equal doses of norephinephrine and epinephrine produce almost identical increments in myocardial contractile force. Cardiac output does not increase after norepinephrine administration because augmented systemic vascular resistance results in reflex bradycardia and diminished cardiac output despite the increased myocardial contractile force. Epinephrine, however, tends to diminish peripheral resistance, and heart rate increase is unopposed by a stimulation of baroceptors. Cardiac output thus rises with increases in myocardial contractile force of a similar magnitude to those produced by norepinephrine. Mephentermine and metaraminol produce increase in myocardial contractile force of a magnitude similar to norepinephrine but of longer duration.

Sympathomimetic amines that increase arterial blood pressure in man may thus be divided into 3 classes: class I amines, such as norepinephrine and epinephrine, increase myocardial contractility and have a short duration of action; class II amines, such as methoxamine, have little or no effect on myocardial contractility and act longer; and class III amines, mephentermine and metaraminol, increase contractility and have an action of long duration.

(Continued on page 44A)

WHY COLLOID BATHS FOR WINTER ITCH?

DRY SKIN
SENILE PRURITUS
BATH ITCH

Cool, low-humidity winter weather brings with it many dry, itching skin conditions such as "winter itch," "dry skin dermatitis" or "senile pruritus."

To control the itching and soften the skin, "The best therapeutic approach is one which hydrates and lubricates the skin."[1]

AVEENO OILATED baths afford relief in one easy step . . . they hydrate the dry epithelium and, at the same time, supply a protective after-bath film of oil to the skin.

The AVEENO OILATED bath supplies colloidal oatmeal saturated with 35% emollient oils. In addition, the colloidal oatmeal has antipruritic and anti-inflammatory effects that are not found in ordinary bath oils.[2-4]

AVEENO® OILATED

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References: 1. Burgoon, C. F., and Burgoon, J. S.: Geriatrics 13:391 (June) 1958. 2. Dick, L. A.: To be published. 3. Franks, A. G.: Am. Pract. & Digest. Treat. 9: 1998 (Dec.) 1958. 4. Senear, F. E., and Haeberlin, J. B., Jr.: in M. Clin. North America, March 1958, pp. 489-496.

2 TYPES OF AVEENO COLLOID BATHS ARE AVAILABLE:

AVEENO® COLLOIDAL OATMEAL
for "wet" or inflamed dermatoses

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for "dry" or chronic dermatoses

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because
DIABETES IS FOR LIFE
start with **Diabinese®**
BRAND OF CHLORPROPAMIDE

for maximum assurance
of continuing success
with oral therapy

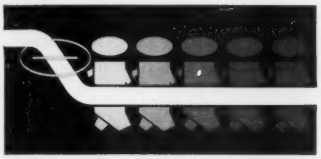
long-term use continues to demonstrate that DIABINESE

has a comparatively low incidence of secondary failures.

provides maximum convenience and economy because of *once-a-day* oral administration.

at presently recommended dosage has a low incidence of adverse effects which require discontinuance of therapy. See "In Brief."

when more than "diet alone" is needed by the maturity-onset diabetic



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the oral antidiabetic most likely to succeed

economical once-a-day dosage

IN BRIEF

DIABINESE, a potent sulfonylurea, provides smooth, long-lasting control of blood sugar permitting economy and simplicity of low, once-a-day dosage. Moreover, DIABINESE often works where other agents have failed to give satisfactory control.

INDICATIONS: Uncomplicated diabetes mellitus of stable, mild or moderately severe nonketotic, maturity-onset type. Certain "brittle" patients may be helped to smoother control with reduced insulin requirements.

ADMINISTRATION AND DOSAGE: Familiarity with criteria for patient selection, continued close medical supervision, and observance by the patient of good dietary and hygienic habits are essential.

As with insulin, DIABINESE dosage must be regulated to individual patient requirements. Average maintenance dosage is 100-500 mg. daily. For most patients the recommended starting dose is 250 mg. given once daily. Geriatric patients should be started on 100-125 mg. daily. A priming dose is not necessary and should not be used; most patients should be maintained on 500 mg. or less daily. Maintenance dosage above 750 mg. should be avoided. Before initiating therapy, consult complete dosage information.

SIDE EFFECTS: In the main, side effects, e.g., hypoglycemia, gastrointestinal intolerance, and neurologic reactions, are related to dosage. They are not encountered frequently on presently recommended low dosage. There have been, however, occasional cases of jaundice and skin eruptions primarily due to drug sensitivity; other side effects which may be idiosyncratic are occasional diarrhea (sometimes sanguineous) and hematologic reactions. Since sensitivity reactions usually occur within the first six weeks of therapy, a time when the patient is under very close supervision, they may be readily detected. Should sensitivity reactions be detected, DIABINESE should be discontinued.

PRECAUTIONS AND CONTRAINDICATIONS: If hypoglycemia is encountered, the patient must be observed and treated continuously as necessary, usually 3-5 days, since DIABINESE is not significantly metabolized and is excreted slowly. DIABINESE as the sole agent is not indicated in juvenile diabetes mellitus and unstable or severely "brittle" diabetes mellitus of the adult type. Contraindicated in patients with hepatic dysfunction and in diabetes complicated by ketosis, acidosis, diabetic coma, fever, severe trauma, gangrene, Raynaud's disease, or severe impairment of renal or thyroid function.

DIABINESE may prolong the activity of barbiturates. An effect like that of disulfiram has been noted when patients on DIABINESE drink alcoholic beverages.

SUPPLIED: As 100 mg. and 250 mg. scored chlorpropamide tablets.

More detailed professional information available on request.

Science for the world's well-being®

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The effects of sympathomimetic amines on myocardial contractile force were determined with the Walton-Brodie strain-gauge arch in 16 patients undergoing operations for congenital heart disease. The effects of sympathomimetic amines on the heart in man were noted to be qualitatively the same as in the dog.

Subdural Hematoma in Older Patients

I. PERLMUTTER. J.A.M.A. 176: 212-214, 1961.

Progressive drowsiness, often with Babinski signs and deterioration of the state of responsiveness, in elderly patients should suggest subdural hematoma. Recognition of this condition in old people is impeded by inadequate history, concomitant intrinsic brain damage, toxic dehydration, senile dementia, and general brain atrophy. Physical evidence of head injury may be absent. Neurologic evidence of increased intracranial pressure may be less prominent in old than in young patients because subdural hematomas become established within dilated subarachnoid spaces. Although characteristic of subdural hematoma in young persons, increase in blood pressure, slowing of pulse, and irregularity and stertorousness of respirations may be absent in older patients. Xanthochromia of the cerebrospinal fluid is present in most cases but may be overlooked if the fluid is examined by artificial light or not compared with an equal quantity of tap water in a similar container.

Glucagon as a Regulating Factor of Plasma Lipids

E. PALOYAN and P. V. HARPER, JR. Metabolism 10: 315-322, 1961.

Glucagon appears to be an important factor in regulating blood lipids. Ablation of glucagon-secreting alpha cells of the pancreas results in extreme hyperlipemia, which is corrected by administration of glucagon parenterally.

In 18 dogs, partial pancreatectomies of various types were performed. The islets of Langerhans in the body and tail of the pancreas of the dog contain alpha cells, whereas the uncinate process and the part of the gland drained by the lesser pancreatic duct are largely devoid of alpha cells in the islets. In dogs with surgical removal of portions of the gland containing alpha cells, extreme hyperlipemia occurred when a small remnant of pancreas was left to supply pancreatic juice to the bowel. No such hyperlipemia occurred when the remnant contained significant numbers of alpha cells.

The hyperlipemia was abolished by the daily intramuscular injection of 10 mg. of crystalline glucagon in oil, and the lower lipid level was maintained as long as injections of glucagon continued. While all hyperlipemic animals showed some degree of diabetes requiring insulin, no apparent relationship was noted between the level of plasma lipids and the insulin dosage. The hyperlipemia was resistant to starvation of four days' duration and to variations in blood sugar.

Tersavid (RO 4-1634), An Amine Oxidase Inhibitor, for the Treatment of Angina Pectoris

S. J. WEISMAN and S. A. WEISMAN. Dis. Chest 39: 459-463, 1961.

Tersavid, an analog of iproniazid, is an effective, low-toxic agent for the prevention and treatment of angina pectoris. Tersavid is a monamine oxidase inhibitor, but the precise mode of action of the drug has not yet been established.

The dosage of Tersavid must be based on the patient's needs and reactions. Generally, 25 mg. for four days followed by a daily maintenance dose of 12.5 mg. gives good results. No attempt should be made to prevent all angina by increasing the dosage of the drug, for without the forewarning of anginal pain, a false sense of security may result in a patient's exertion to the point of danger.

Tersavid was used in the treatment of

(Continued on page 48A)

"nervous indigestion" is this patient's complaint

antispasmodic
-sedative
-digestant

Donnazyme®

This old gentleman is fictitious but his problem is not. In fact, the label he aptly tags his symptoms with might even suit one or two of your patients. If they are tense or mildly anxious, and you find a functional or ill-defined gastrointestinal spasm and an inadequate supply of digestive enzymes, that is "nervous indigestion." For these conditions, Donnazyme offers specific medication which relieves GI spasm, calms the emotions, and supplements deficient digestive enzymes. Two tablets t.i.d. (after meals), or as needed.

Each specially constructed tablet contains the equivalent of one-half Donnatal® tablet plus digestive enzymes. **In the gastric-soluble outer layer:** hyoscyamine sulfate, 0.0518 mg.; atropine sulfate, 0.0097 mg.; hyoscine hydrobromide, 0.0033 mg.; phenobarbital (1/8 gr.), 8.1 mg.; and pepsin, NF, 150 mg. **In the enteric-coated core:** pancreatin, NF, 300 mg.; and bile salts, 150 mg.

A. H. Robins Company, Inc.
RICHMOND 20, VIRGINIA

"nutrition . . . present as a modifying or complicating factor in nearly every illness or disease state."[1]

Theragran®

Squibb Vitamins for Therapy

clinically-formulated and potency-protected vitamins for your patients with degenerative diseases who need therapeutic vitamin support

"Studies by Wexberg, Jolliffe and others have indicated that many of the symptoms attributed in the past to senility or to cerebral arteriosclerosis seem to respond with remarkable speed to the administration of vitamins, particularly niacin and ascorbic acid. These facts indicate that the vitamin reserve of aging persons is lowered, even to the danger point, more than is the case in the average American adult."[2]

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Vitamin A	25,000 U.S.P. Units
Vitamin D	1,000 U.S.P. Units
Thiamine Mononitrate	10 mg.
Riboflavin	10 mg.
Niacinamide	100 mg.
Vitamin C	200 mg.
Pyridoxine Hydrochloride	5 mg.
Calcium Pantothenate	20 mg.
Vitamin B_{12}	5 mcg.

For full information see your Squibb Product Reference or Product Brief.

1. Youmans, J. B.: Am. J. Med. 25:659 (Nov.) 1958. 2. Overholser, W., and Fong, T. C. C. in Stieglitz, E. J.: Geriatric Medicine, 3rd edition, J. B. Lippincott, Philadelphia, 1954, p. 264.

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Squibb Quality—the Priceless Ingredient

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Where's the arthritic this morning?

Thanks to Medrol Medules, he woke up comfortable and he's already on the go.

The first long-acting oral steroid, Medrol Medules gives the arthritic patient therapeutic action that continues through the night. In many cases, morning stiffness can become a thing of the past.

The slow, steady release of methylprednisolone often provides greater effectiveness, with less frequent administration and sometimes a reduced total daily dosage.

Many of your arthritic patients, too, can wake up comfortable on Medrol Medules.

Dosage: The following dosages are recommended in rheumatoid arthritis:

	Initial	*Maintenance*
Severe	12 to 16 mg.	6 to 12 mg.
Moderately severe	8 to 10 mg.	4 to 8 mg.
Moderate	6 to 8 mg.	2 to 6 mg.
Children	6 to 10 mg.	2 to 8 mg.

With Medrol Medules, it may be possible to reduce the total daily dose by ½.

Indications and effects: Medrol benefits (anti-inflammatory, antiallergic, antirheumatic, antileukemic, antihemolytic) have been demonstrated in acute rheumatic carditis, rheumatoid arthritis, asthma, hay fever and allergic disorders, dermatoses, blood dyscrasias, and ocular inflammatory disease involving the posterior segment.

Precautions and contraindications: Because of Medrol's high therapeutic ratio, patients usually experience dramatic relief without developing such possible steroid side effects as gastrointestinal intolerance, weight gain or weight loss, edema, hypertension, acne, or emotional imbalance.

As in all corticotherapy, however, there are certain cautions to be observed. The presence of diabetes, osteoporosis, chronic psychotic reactions, predisposition to thrombophlebitis, hypertension, congestive heart failure, renal insufficiency, or active tuberculosis necessitates careful control in the use of steroids. Like all corticosteroids, Medrol is contraindicated in patients with arrested tuberculosis, peptic ulcer, acute psychoses, Cushing's syndrome, herpes simplex keratitis, vaccinia, or varicella.

Approximately 135 tiny "doses" mean smoother steroid therapy

Medrol* Medules*

Each capsule contains: Medrol (methylprednisolone) 2 mg. or 4 mg. Supplied in bottles of 30 and 100.

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JUNE, 1961

THE UPJOHN COMPANY, KALAMAZOO, MICHIGAN

31 patients with angina pectoris, with results ranging from good to poor. Liver function tests and blood studies gave no indication of drug toxicity, and no evidence was found of jaundice, gastrointestinal disturbances, blood dyscrasias, syncope, or cardiographic changes. Untoward reactions of vertigo and orthostatic hypotension were found in 2 patients. Myocardial infarctions resulted in 3 deaths. That the drug contributed to these deaths by causing periods of marked hypotension is a remote possibility, but the age and long history of cardiac disease of the patients allowed for death without iatrogenic contribution.

Ocular Causes of Vertigo in the Geriatric Patient

D. SNYDACKER. J. Louisiana M. Soc. 113: 217-220, 1961.

Vertigo of ocular origin may occur after a sudden change in the way in which objects are visually perceived. Extraocular muscle paresis or paralysis, diplopia, a sudden change in the vision of one eye as a result of a retinal lesion in or around the macular region, or new glasses may be the cause.

In complete paralysis of the oculomotor or abducens nerves, diagnosis may be made by examination of the eyes as the patient follows a moving object into the various fields of gaze. Lesion of the oculomotor nerve results in drooping of the eyelid and a downward and outward deviation of the eye. The pupil is usually dilated. The globe moves little or not at all and the eye is fixed in the down and out position.

Lesion of the trochlear nerve limits the field of action of the eye. In paresis or trochlear nerve paralysis, closing of the affected eye eliminates diplopia and vertigo, while closing of the unaffected eye eliminates diplopia but not vertigo.

Impaired function of extraocular muscles may be due to tumors; aneurysms or neoplasms, which mechanically interfere; or trauma of the orbital structures. Diagnosis is made by inspection. A patient with diplopia will see a red and a white image when a red glass is held over one eye while he looks at a small light. Patients with head injury or uni- or bilateral subconjunctival hemorrhage should be checked for diplopia.

Senile Type Body-Water Changes in Degenerative Diseases of the Central Nervous System in Middle-Aged Subjects

E. WOODFORD-WILLIAMS and D. WEBSTER. Brit. M. J. 5233: 1126-1127, 1961.

Progressive colloid condensation and reduced water-binding capacity of tissue cells during aging may reflect metabolic changes in the colloids. In patients with degenerative central nervous system diseases, cellular colloid condensation may appear before old age. Involvement of the diencephalon, part of a feed-back mechanism regulating food intake, endocrine activity, and metabolism, may account for earlier colloid condensation.

Three groups, consisting of (1) 22 healthy persons aged 40 to 59 years, (2) 10 healthy persons aged 80 to 89 years, and (3) 7 patients with degenerative central nervous system diseases aged 40 to 49 years were investigated. Mean total body water and lean body mass were significantly greater only in the healthy middle-aged group. Volume of extracellular water was similar in all groups.

Mucolytic Expectorant Therapy with an Iodinated Glyceryl Ether

A. SELTZER. Ann. Allergy 19: 381-385, 1961.

An iodinated glyceryl ether (Organidin) appears to be superior to and to have less adverse side effects than potassium iodide in the treatment of asthma, emphysema, and bronchitis. With the iodinated glyceryl ether, the total iodine intake can be reduced to one-twentieth of that necessary when using potassium iodide, thus greatly

(Continued on page 52A)

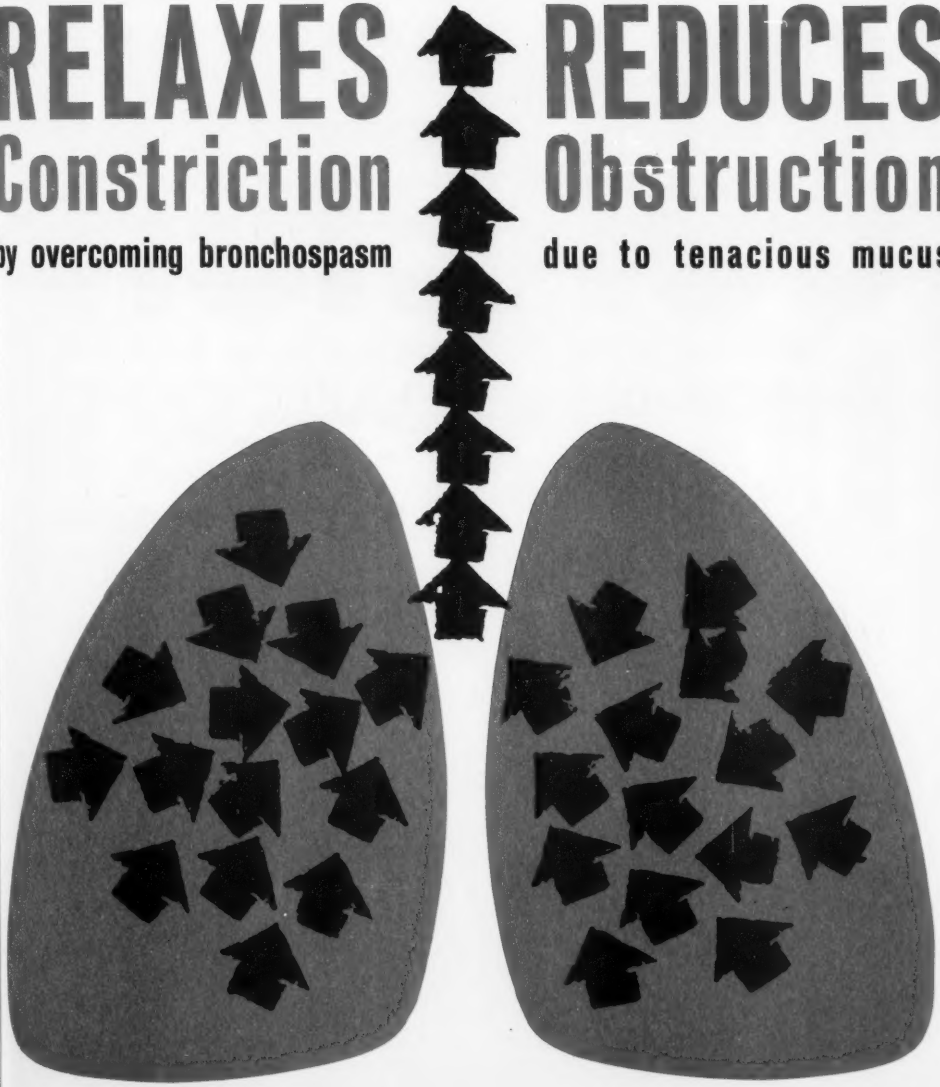
Announcing a new product for the management of asthma

RELAXES Constriction

by overcoming bronchospasm

REDUCES Obstruction

due to tenacious mucus



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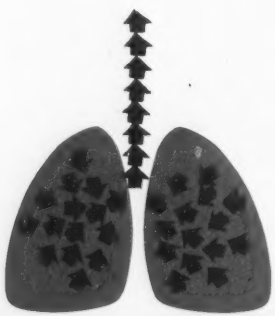
BRONCHODILATOR-EXPECTORANT

RELAXES CONSTRICTION by overcoming bronchospasm

Theophylline overcomes bronchospasm through relaxation of the bronchiolar smooth muscle.

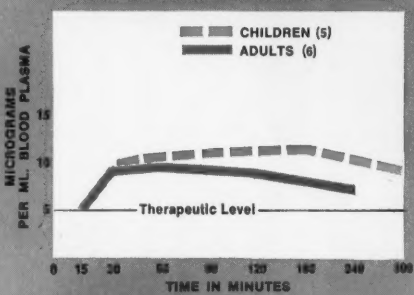
REDUCES OBSTRUCTION due to tenacious mucus

Glyceryl guaiacolate increases respiratory tract fluids which dilute the thick tenacious mucus in the bronchioles, facilitating its removal and thereby reducing obstruction.



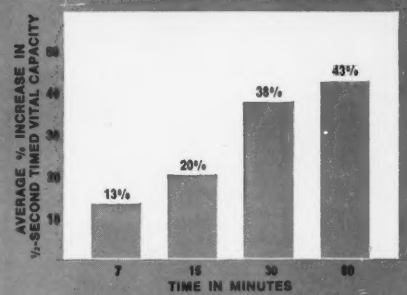
- combines the bronchodilator effectiveness of theophylline[1-4]
- with the proved expectorant action of glyceryl guaiacolate[5,6]
- formulated for flexible low-volume dosage
- in a pleasant-tasting hydro-alcoholic vehicle for rapid absorption

QUIBRON RAPIDLY PROVIDES EFFECTIVE THEOPHYLLINE BLOOD LEVELS[7,8]



Following administration of Quibron elixir at the recommended dosage for adults[7] and children,[8] effective blood levels of theophylline were reached within 15-30 minutes and maintained for more than four hours.

THERAPY WITH QUIBRON IS FOLLOWED BY RAPID IMPROVEMENT OF VITAL CAPACITY[9]



Following administration of 20 ml. Quibron elixir, vital capacity was markedly improved, as measured by the timed ½-second method. Pulmonary function tests confirmed the clinical observation of rapid relief occurring in 10-15 minutes in most patients.[9]

Indications: Bronchial asthma, asthmatic bronchitis, chronic bronchitis and pulmonary emphysema.

Dosage & Administration: *Adults:* 1 to 2 tablespoons, 2–3 times daily. *Children, 6–12:* 1 tablespoon, 2–3 times daily. (Children weighing over 100 lbs. may require adult doses.) *Children under 6:* ½ teaspoon per 10 lbs. body weight, 2–3 times daily. During the first day of treatment, especially in severe attacks, the usual dose may be increased by one half.

Side Effects: Theophylline may cause gastric irritation, with possible abdominal discomfort, nausea and vomiting. The administration of Quibron elixir after meals may help avoid such symptoms. Theophylline may also exert some stimulating effect on the central nervous system.

Cautions: Quibron elixir should not be administered more frequently than every 6 hours or within 12 hours after rectal administration of any preparation containing theophylline or aminophylline. Other formulations containing xanthine derivatives should not be given concurrently with Quibron elixir.

Supplied: Each tablespoon of Quibron elixir (15 ml.) contains theophylline 150 mg. and glyceryl guaiacolate 90 mg. in a 15% hydro-alcoholic vehicle. Bottles of 8 fl. oz.

References: (1) Schluger, J.; McGinn, J. T., and Hennessy, D. J.: Am. J. M. Sc. *233*:296-302 (March) 1957. (2) MacLaren, W. R.: California Med. *91*:278-282 (Nov.) 1959. (3) MacLaren, W. R.: Ann. Allergy *17*:729-739 (Sept.-Oct.) 1959. (4) Spielman, A. D.: Ann. Allergy *15*:270-276 (May-June) 1957. (5) Cass, L. J., and Frederick, W. S.: Am. Pract. & Digest Treat. 2:844-851 (Oct.) 1951. (6) Schwartz, E.; Levin, L.; Leibowitz, H., and McGinn, J. T.: Am. Pract. & Digest Treat. 7:585-588 (April) 1956. (7) Schiller, I. W., and Goldman, G.: Personal communication on file at the Mead Johnson Research Center.* (8) Levin, S. J., and Weisnagel, J.: Personal communication on file at the Mead Johnson Research Center.* (9) Puls, R. J., and Grater, W. C.: Current Therap. Res., in press (Nov.) 1961.

*These data are available to physicians on request.

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Parkinson's disease does not have to mean a retreat from living or reluctance to face family and friends. Treatment with "COGENTIN often causes a diminution or disappearance of the typical parkinsonian facies. It has the ability to control severe tremor and may control sialorrhea better than atropine."[1] Severe rigidity, contractures, and frozen states also respond to COGENTIN.[2] Its prolonged action permits 24-hour control of symptoms with one bedtime dose.[3]

Before prescribing or administering COGENTIN, the physician should consult the detailed information on use accompanying the package or available on request. Supplied: Tablets COGENTIN (quarterscored), 2 mg., bottles of 100 and 1000. New dose form: Injection COGENTIN, 1 mg. per cc., ampuls of 2 cc., boxes of 6. References: 1. Finkel, M. J.: M. Times 86:1391, 1958. 2. Doshay, L. J., and Boshes, L.: Postgrad. Med. 27:602, 1960. 3. A. M. A. Council on Drugs: New and Nonofficial Drugs 1960, Philadelphia, J. B. Lippincott Company, 1960, p. 264. COGENTIN is a trademark of Merck & Co., Inc.

MSD MERCK SHARP & DOHME Division of Merck & Co., INC., West Point, Pa.

reducing the incidence of iodism and thyroid enlargement. Most iodide-sensitive patients can take the preparation without signs of intolerance.

With effective dosage, the patient receives a total daily amount of iodine of approximately 80 to 120 mg., which does not cause significant changes in the protein-bound iodine measurement. Gastric irritation is not encountered.

Use of the mucolytic-expectorant agent is valuable whenever bronchial conditions are being treated with antihistamines, bronchodilators, and antibiotics, as these agents may cause the sputum to become viscid and thereby impede expectoration. The 5 per cent solution may be used as an aerosol for asthma, emphysema, and asthmatic bronchitis, alone or added to epinephrine or isoproterenol (Isuprel) aerosols. The glycerol aids in producing a stable aerosol of small particle size, and the iodide is nonirritating and acts to liquefy tenacious sputum.

Vocal Rehabilitation of Paralytic Dysphonia

G. E. ARNOLD. Arch. Otolaryng. 73: 290-294, 1961.

Either pure tantalum or tantalum oxide powder suspended in glycerin injected into scar tissue replacing an excised vocal cord or into a paralytic cord restores vocal function. The material is well tolerated by the tissues, will not resorb in time like cartilage and bone dusts, and is injectable through the long needle of a Bruenings syringe. The postoperative course is uncomplicated and short, and voice is restored as well as with paraffin injections.

Both powders can be sterilized by autoclaving in an open container. Before injection, the powder is mixed with a sufficient amount of sterile glycerin to yield a soft injectable paste.

Tantalum powder, 1 cc. suspended in glycerin, injected into the leg muscle of a rabbit was well tolerated. Histologic study nine months later revealed slight foreign-body reaction. Muscle fibers surrounding the implant retained normal striation. Several patients with unilateral laryngeal paralysis and with insufficient glottal closure after chordectomy were treated with good results.

Intravenous Hypertonic Urea in the Management of Acute Angle-Closure Glaucoma

K. HILL, J. B. WHITNEY, and R. R. TROTTER. Arch. Ophth. 65: 497-503, 1961.

Intravenous infusion of hypertonic urea in doses of about 1 gm. per kilogram of body weight will produce prompt fall in intraocular pressure by osmotic action. A solution of 30 per cent lyophilized urea with 10 per cent invert sugar is given over a period of approximately ninety minutes. Transient confusion and agitation may follow if the solution is administered too rapidly.

In 13 patients with acute angle-closure glaucoma, intraocular pressure was reduced in 10 eyes to 23 mm. Hg or less four hours after intravenous infusion of hypertonic urea. In 3 eyes, the lowest pressure reached was 40 to 45 mm. Hg. Local phlebitis appeared in 2 patients. Headache occurred in 5 patients, and several complained of thirst.

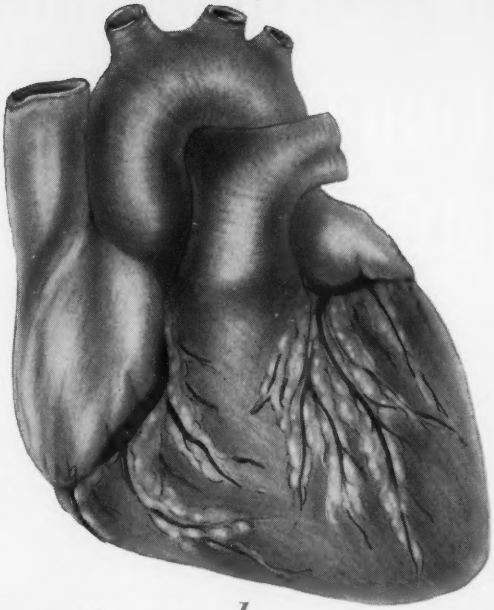
Current Concepts of Myalgia of the Head

R. E. RYAN. Eye, Ear, Nose, & Throat Month. 40: 119-121, 1961.

Myalgia of the head, unlike vascular headaches, has a gradual onset and subsidence. The pain is caused by spasmodic contraction of the arterial end of the affected muscular capillaries with resultant ischemia and is usually localized to a circumscribed area of the musculature of the head which becomes very tender to touch and pressure. Two groups of muscles may be involved: the postural muscles inserting into the

(Continued on page 56A)

coronary insufficiency?



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in angina: "Because of its rapid action...it may be used like nitroglycerin before contemplated exertion or excitement when more prolonged prophylaxis is desired." Russek, H. I.: Am. J. M. Sc. *239*:478, 1960.

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Mazola Corn Oil is unexcelled in polyunsaturates and lowest in saturates of all leading brands of vegetable oils. Mazola's P/S ratio is far higher than that of any other leading food oil. Your patient will find Mazola Corn Oil ideally suited for salad dressings and frying; also for baking wherever *liquid* shortenings are called for in the recipe.

Mazola Margarine contains *liquid* Mazola Corn Oil as a major ingredient. This corn oil is not hydrogenated, thereby preserving its rich content of linoleates. Mazola Margarine contains 2 to 3 times as much natural linoleates as any other margarine readily available in grocery stores from coast to coast. Its taste, color and handling characteristics are unexcelled.

AVERAGE COMPOSITIONS OF MAZOLA® MARGARINE AND MAZOLA® CORN OIL
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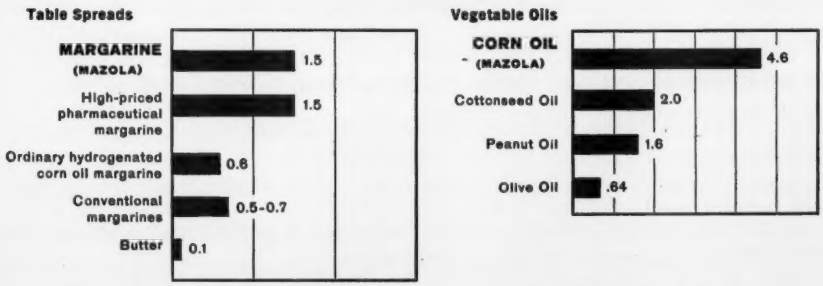
	MAZOLA MARGARINE		MAZOLA CORN OIL	
	100 grams	2 oz. (4 tbsp.)	100 grams	1 fl. oz. (2 tbsp.)
Fatty Acids				
Polyunsaturated	21	12	51	14
Monounsaturated	40	23	32	9
Saturated	14	8	11	3
Natural Sitosterols	0.5	0.3	1	0.3
Natural Tocopherols	0.08	0.045	0.08	0.020
Cholesterol	none	none	none	none
Sodium	0.9	0.5	none	none

MAZOLA MARGARINE—410 Calories/2 oz.; Iodine Value—96
MAZOLA CORN OIL—250 Calories/fl. oz.; Iodine Value—124

RATIO OF POLYUNSATURATES/SATURATES
(Average values.)



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cranial bones, or the muscles with origin from the bones of the skull, particularly the occipitofrontalis and temporalis.

Myalgia of the head is classified as a hereditary physical allergy usually observed in patients sensitive to sudden temperature changes. Thus, myalgic attacks commonly occur in the spring and fall. Exposure to air conditioners, drafts, electric fans, humidity, and atmospheric pressure changes may precipitate attacks. In addition, increased tenseness of the postural muscles and acute infections may occasionally trigger an attack.

Daily intramuscular administration of nicotinic acid (Niacin) is the treatment of choice. Flushing, sensations of warmth and itchiness may be unpleasant but temporary side effects. Acetylsalicylic acid does not relieve the pain—a useful finding in differential diagnosis. Mephenesin is an effective skeletal muscular relaxant. Cotaphen, containing both mephenesin and nicotinic acid, is beneficial; two capsules should be given three times a day during the acute attack. One capsule three times a day and subsequent substitution of 100 mg. of nicotinic acid two or three times daily should be instituted when the pain begins to subside. Methocarbamol (Robaxin), the medcolator, moist heat, and massage may similarly give relief. Prevention of exposure to sudden temperature changes is the best prophylactic against the attacks.

The Fractured Hip, a Complication of Aging

J. MANPEL, V. MARZULLI, and S. J. BOLEY. Arch. Surg. 82: 474-477, 1961.

In patients with fracture of the hip, length of delay before operation is directly proportional to rate of mortality. Age, associated diseases, and complications of operation also influence mortality.

In general, fractured hips should be pinned; fixation should be done within seventy-two hours, if possible. The general aim is to have the patient out of bed and in a chair the day after operation. Early ambulation and activity always are attempted.

Of 361 women and 135 men with acute fracture of the hip treated from 1955 to 1958, 412 had one or more associated diseases, 172 had one or more postoperative complications, and 132 died. Average age was 75.9 years, and average stay in the hospital was about forty days. Hips were pinned in 426 of the patients. Of the 70 patients who, because of serious associated disease, were not operated on, 55 died in the hospital.

Only 6 of the 132 patients who died did not have associated disease, whereas 49 had at least 2 such diseases, most of which were cardiovascular or pulmonary. For all patients, the average delay from admission to operation was 7.3 days; among patients who died, the delay was 7.9 days. While 140 of all patients were not given antibiotics preoperatively, 50 of the 132 patients who died did not receive the drugs. The incidence of complications among patients who died was double the over-all incidence.

Errors in the Diagnosis of Rheumatic and Congenital Heart Disease in Elderly Patients

M. L. RUSK. Stanford M. Bull. 19: 32-34, 1961.

Valvular and congenital defects in old patients often are masked or imitated by coronary atherosclerosis and hypertension. The course and findings may differ from the accepted course and findings of the same conditions in young patients.

Typical signs of rheumatic heart disease—auricular fibrillation, murmurs of mitral stenosis, insufficiency, and left atrial hypertrophy—may be noted in an occasional patient. Usually, however, the diagnosis must depend on such isolated observations as rheumatic systolic murmur, irregular cardiac rhythm, right bundle-branch block, and left atrial enlargement with general cardiomegaly or calcification of one or more valves.

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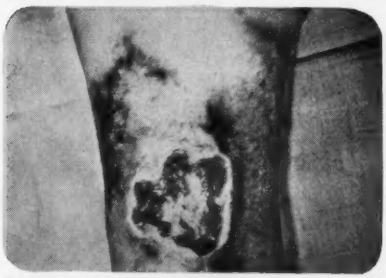

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1. Bovet, D., and Nitti-Bovet, F.: Arch. Internat. de pharmacodyn. et therap. 83:367, 1946. 2. Melville, K.I., and Lu, F.C.: Canad. M.A.J. 65:11, 1951. 3. Fuller, H.L. and Kassel, L.E.: Antibiotic Med. & Clin. Therapy 3:322, 1956. 4. Eisfelder, H.W. et al.: J. Am. Geriatrics Soc. 8:62, 1960.

1 tablet all day

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Geriatrics Volume 16—Number 11

Editorials

More on nursing homes for the aged

▶ In an excellent article, "The Proprietary Nursing Home—A Statistical Evaluation," Dr. Elkin Ravetz, who practices in Philadelphia, says that nursing homes should relieve the pressure on hospitals. They should promote a free interchange of patients between the homes and the hospitals and should take care of those many patients who, on leaving a hospital, for one reason or another cannot go straight home. The homes should provide facilities for the terminal patient who can no longer benefit from hospitalization, with all its curative technics. They should provide cheerful and pleasant surroundings for the short-term convalescent patients. They can, at times, take care of an invalid for a period during which his family is perhaps away from home or in need of a rest.

The nursing home should be geared for rapid (emergency) admissions. The importance of this is brought out when a family suddenly finds on its hands a relative with a severe stroke and then learns that there is no room anywhere for him.

Whenever possible, nursing homes should encourage the return of the old patient to his family. Nursing homes should not be just places in which unfortunates can go while they are waiting to die. The homes should be attractive, bright and cheerful in both building and grounds, if only to neutralize some of the terrible feelings of guilt that may be felt by the patient's relatives for having "put him away." Although, doubtless, in the years to come, there will be great demands made on cities and states to construct huge institutions of a type between an old peoples' home and a hospital, Dr. Ravetz believes that private enterprise will do the better job. Private enterprise should be able to provide many of the institutional needs of the sick and the aged with greater humanity and efficiency and at less cost to the taxpayer.

WALTER C. ALVAREZ, M.D.

Current comment

Radiation and aging: a review

▶ A symposium report has recently appeared on radiation and aging which summarizes panel discussions held during the past few years organized by the American Institute of Biological Sciences, with the support of the Center for Aging Research of the National Institutes of Health and the Division of Biology and Medicine of the Atomic Energy Commission. It was published in July 1961 by the Federation of American Societies for Experimental Biology in *Federation Proceedings*. The symposium is brilliantly introduced and summarized by Philip Handler, Professor of Biochemistry at Duke University, who was editor for the publication. An attempt will be made to outline the significant aspects of this discussion.

Dr. Handler points out, in his introduction, that studies on the influence of high-energy radiation on animals, stimulated by the terrifying biologic effects of atomic bombing, show that irradiated animals which survive the acute radiation syndrome exhibit a significantly decreased life expectancy. The incidence of neoplasia in such animals is increased, but this is insufficient to account for the generally observed decreased life span. When tumor-bearing animals are discounted, the causes of death in the irradiated animals are not statistically different from those observed in ordinary aging animals. Hence it was suggested that radiation causes "a general acceleration of the normal aging process."

Striking parallelisms emerge when one observes normal aging animals in relation to irradiated animals: (1) life expectancy is decreased in a linear manner with increasing time; (2) the incidence of leukemia is increased as a linear function of time, and there is an increasing incidence of malignancy; (3) there is a reduced resistance either to infection or to subsequent radiation; and, in general, (4) there tends to be no specific organ, tissue, or physiologic function in which a primary defect occurs but rather a general deterioration in many tissues.

The panel discussions resulted in some general conclusions: (1) aging is a situation in which catabolism becomes dominant over anabolism, with resulting decrease in functional capacity; (2) aging seems to be a change in constitution due to an inequality in the rates of appearance and disappearance of specific structures, with changes which are not directed toward the production of a more effectively adapted organism; (3) the mathematic description of the aging rate in any species is provided by an equation, originally formulated by Gompertz, which includes a constant which seems to be genetically built in for each biologic species; and (4) as suggested by Nathan Shock, the time-dependent decline in the function of many organ systems in mammals reflects the simple loss of postmitotic cells in nondividing tissues, which is ex-

pressed as a decrease in vital capacity, in muscle strength, in renal function, in mental acuity, and in cardiac activity; at the same time, there is little decrease in the activity of bone marrow or liver, which consist of tissues in which mitosis remains the same throughout life.

Similarities between physiologic and radiologic aging. Thomas F. Daugherty of the Department of Anatomy at the University of Utah College of Medicine summarizes the discussions reviewing similarities between physiologic and radiologic-accelerated aging. There seem to be 3 ways by which x-rays and other types of chronic radiation may shorten life: (1) by increasing the production of diseased conditions, such as neoplasms; (2) by inhibiting adequate repopulation of transient tissues; and (3) by accelerating the rate of appearance of degenerative alterations in various tissues.

Irradiation seems to accelerate no single change in tissues but rather a wide variety of age-dependent, pathologic changes similar to those expected during the usual aging process and unique to particular species. Both radiation and aging seem to injure certain susceptible cells which may trigger waves of cellular destruction through an accumulation of cytotoxic debris. For instance, cells of the crypts of Lieberkühn in the intestine are highly susceptible to radiation and also to aging; once these are injured, the intestinal secretions may be so reduced that there is a lack of adequate enzyme production, which interferes with digestion and thus may cause a long series of secondary effects. In cellular injury, whether from radiation or from repeated stress, as in aging, cytotoxins such as histamine may be released and may set off a series of secondary effects, which result in various aspects of malfunctioning.

After cellular damage has been produced, either by repeated stress or by exposure to radiation, there comes a phase of repair, which is reduced both by aging and by radiation. If the germinal element in proliferating cells is injured, as in radiation, there will be unsatisfactory repair. This also occurs as a result of repeated stress, as in aging. The margin of cellular reserve becomes less in older individuals as well as in chronic irradiated individuals.

Both the vascular bed and the blood volume in mammals diminish during aging and after radiation. Under these circumstances, additional stresses may tax the individual organism beyond its capacity. Progressive deterioration of the various tissues of the body seems to occur as a result both of multiple accumulating stress effects during life and of exposure to various types of radiation.

Lymphatic tissues change with time in a definite sequential fashion. There is a rapid prepubertal growth, which quickly declines after puberty but continues to diminish at a rather steady rate during the rest of the life span. Lymphatic tissue is the only tissue in the mammalian body which behaves in this manner. Lymphatic tissue is exceedingly sensitive to radiation, as well as to adrenocortical hormones. Both radia-

tion and corticosteroids tend to destroy lymphocytes, and this effect is followed by rapid reconstruction to an amount of lymphatic tissue characteristic for the age of the animal. There thus appears to be a lymphatic tissue time clock. This is reflected in the age-involution of the thymus as well as other lymphatic tissue.

Both radiation and corticosteroids seem to inhibit antibody and gamma-globulin synthesis. This inhibition tends to reduce further the functional capacity for regeneration in injured tissues.

▶ *Biochemical and radiation time relations on living systems.* Philip Handler well reviews the panel discussion on biochemical aspects of possible relationships between the biologic effects of radiation and the normal process of senescence. It does not seem correct to say that radiation accelerates aging. The data show that irradiated animals "age" months or years within a few minutes after radiation. The time phenomenon responsible for life shortening in radiated animals appears to be damage to cell nuclei. There is evidence that chromosomal damage after radiation persists, so that regeneration of injured tissue is altered.

The panel agrees with Nathan Shock's evidence that there is no significant difference between the metabolic functioning of old and young tissues in respect to oxygen consumption, tissue-enzyme activity, or the circulating level of various metabolites. On the other hand, older mammals invariably exhibit a relatively sluggish response to physical or metabolic stresses. The best explanation of the functional impairment of aging tissues is an absolute loss in cell population, with replacement of lost cells by extracellular fluid or by connective tissue.

Many hypotheses were explored by the panel in order to explain the progressive time-dependent cell deterioration in aging animals. The most attractive theory seems to be that cell death results from a gradually depleting supply of metabolites or a gradual reduction in the rate of removal of metabolic products. Normal aging may be the penalty which a complex organism pays for its multicellularity.

Multicellular animals are distinguished from unicellular organisms, such as bacteria, by the separation of their cells from their food supply and from the atmosphere by connective tissue. This connective tissue increases in aging, and as it increases, it interferes more and more with the passage of food into the cells and of waste materials away from the cells. With this interference of metabolic flow, the increasing connective tissue may gradually result in blocking cellular function.

Much biochemical study is being undertaken on connective tissue. This may help us to learn the various complex factors that are concerned in the gradual growth of connective tissue as the aging process proceeds. This study may be helped by observing the changes in connective tissue which result from deliberate and controlled radiation.

▶ *Physiologic aging and radiologic life shortening.* Laurence W. Kinsell of the Institute for Metabolic Research in Oakland, California, sum-

marizes the panel discussion of the physiology group. A quantitative approach to aging in organs or tissues, whether from repeated stress or radiation, may be based on the decrease in the total number of cells in specific organs or tissues and in the decrease in functional capacity of such organs or tissues with time as compared to the maximal number of cells or optimal functional capacity of some earlier period in the life span. This sort of quantitative approach may show clearly the parallels between physiologic aging and radiation injury.

After detailed consideration of the various functional activities of different organs in the mammalian body as they change with age or after radiation, the group concludes that some degree of simplification is necessary in order to approach the problem scientifically. It is agreed to use the gradual decrease in total cell population in any given organ or tissue as a quantitative manifestation of aging. Adequate means to measure qualitative changes which accompany aging are not yet available. Controlled radiation of specific quantitative kinds, such as x-rays or ultra-violet light, seems to be possible as an experimental tool for the study of physiologic aging. Objective criteria are necessary to measure adequately either physiologic aging or radiation effects. The results of such measurements may help in revealing the underlying mechanisms involved.

▶

Changing rates of aging. Ralph W. Brauer of the U.S. Radiologic Defense Laboratories at San Francisco summarizes many of the difficulties involved in studying changing rates of aging, particularly in reference to the latent effects of radiation exposures. He emphasizes the significant fact that many of the criteria of aging are subject to environmental influences. Sex differences in life expectancy also are important, and the factors involved are not yet clear.

A unified concept of aging remains elusive. If aging is viewed as the accumulation, over an individual life span, of irreversible cellular and integrative changes, then the experimental study of aging must deal with those separate processes by which the organism as a whole loses its ability to repair or restore any part of itself or of its integrative functions or to rebalance its metabolism. Any attempt to study aging by experimental modification becomes a useful tool only in proportion to its value in revealing the mechanisms of injury or disease.

By using radiation, one may study specific cellular and organic integrative changes under controlled time conditions. But, again, all the complex factors involved in the environment are pertinent. This point of view emphasizes the significance of the whole ecologic milieu as a factor in the aging process and in the response to radiation. This further emphasizes the importance of considering carefully the different aspects of biologic functioning at different levels of biologic organization.

▶

Cellular aspects of radiation and aging in mammals. T. T. Puck of the Department of Biophysics at the University of Colorado Medical

Center in Denver summarizes the discussion on radiation and aging manifestations at a cellular level. He points out that the aging process, like chronic, low-level irradiation in mammals, produces degenerative cellular changes which are not clearly defined. In both instances, (1) the mortality rate increases as a direct function of the amount of aging or irradiation; (2) it has not been possible to find any particular organ, tissue, or function in which a primary defect occurs but rather there appears to be a general loss of physiologic efficiency in most tissues; and (3) there is an increase in the frequency of malignancy.

This suggests that the basic effect in both aging and radiation has to do with events at a cellular level of biologic organization. Certainly, radiation is well-known to involve genetic damage. Whether or not aging involves genetic factors remains to be examined.

This matter is further explored by a special genetics panel under the chairmanship of John W. Gowen of the Department of Genetics at Iowa State University of Science and Technology at Ames. In this panel, various inheritance patterns are considered in relation to senescence, and special emphasis is placed on somatic mutations as a direct means of altering an organism's genotype as it ages. There is discussion on chemical aspects of somatic cross-over and on cytoplasmic-nuclear interactions. The genetic similarities between the development of senescence and the effects of radiation exposure are discussed. Special attention is given to somatic dominant-gene mutations. As these occur, they create a mosaic of cells in which lethal changes take place, leading to necrosis of cells, with resulting accumulation of cellular debris which interfers with the functional activity of the normal cells remaining. H. J. Muller discusses the significance of chromosome breakage as an aspect of somatic damage produced by radiation and possibly occurring in aging.

▶

Miscellaneous. Hardin B. Jones of the Donner Laboratory of the University of California at Berkeley stresses the accumulation of radiation effects at small exposures. He points out that the blood-forming tissues are inherently sensitive to radiation but that this is not necessarily a common aspect of aging.

An interesting observation is reported by O. H. Robertson of Stanford University to the effect that maturation of gonads in such organisms as salmon may result in lethal physiologic disturbances. In general, the life span of castrated salmon is prolonged.

▶

Summary. Philip Handler summarizes the symposium in an excellent manner. He points out that the genetic apparatus of cells is damaged in postirradiated animals and that this must surely diminish the reserve of the stem lines of proliferating tissue and hence enhance the susceptibility to further radiation or stress. Normal senescence also reflects the loss of cells in undividing tissue. Cellular death may be occasioned by alteration in connective tissue, particularly of capillaries.

The delayed effects of radiation on the one hand and of normal senescence on the other may appear to be equivalent to the extent that time-dependent deterioration of the capillaries of postirradiated animals, as in the case of old animals, may account for the gradual death of post mitotic cells in all tissues of the body. This results in a diffused deterioration of practically all tissues, so that the immediate causes of death are varied. It appears that the connective tissue barrier between parenchymatous cells and their surroundings may undergo a time-dependent deterioration both in aging and as a result of radiation. On this basis, mortality is a built-in biologic penalty for the multicellular existence of higher organisms.

Common both to the normal aging individual and to the postirradiated mammal is arteriolocapillary fibrosis, which may occur directly as a result of radiation or as an accumulation of the diversity of stresses which the environment may impose on the organism. Chromosomal damage to somatic cells may thus occur indirectly in the case of aging but more directly in the case of exposure to radiation. Thus there may be justification for an analogy between the effects of radiation and of aging, but it remains a matter of choice whether the resemblances or differences are to be emphasized.

* * * * *

Obviously, this is an extremely important scientific analysis of the biologic processes occurring both in aging and in exposure of living material to radiation. Significant conclusions are certain to develop as a result of further study. For example, the importance of quinones in electron transport, and their significance at a cellular level for energy production and for regeneration, suggest that they be investigated with respect to what occurs to their tissue concentrations as a result either of exposure to radiation or of natural aging. Specific chemical agents may be found that can counteract both the harmful effects of radiation and the natural deterioration occurring with age. But what then? As we extrapolate to ourselves, do we want to live longer if the living is not worthwhile? Or do we wish to disturb further the exquisitely poised delicate balance of nature, which has evolved over millions of years, with further disastrous results of overpopulation?

CHAUNCEY D. LEAKE

ROBERT W. BOYLE, PH.D., M.D.
Professor, Department of Physical Medicine, Marquette University School of Medicine, Milwaukee, and director, Department of Physical Medicine and Rehabilitation, Milwaukee County Hospital

Control of chronic pain in the elderly patient

Control of chronic pain in the elderly patient is more dependent upon an understanding of the patient than upon selection of a drug to relieve the pain. Chronic pain is a complex of many experiences involving acute pain, each of which has its own set of circumstances. The solution to the patient's distress must be based on an understanding of the relationship of the past experiences to the present circumstances.

▶ The awareness of acute pain transmitted as a message to the conscious centers is well known as a defense mechanism. It informs the recipient that something must be done to get away from the harmful stimulus. When the pain is received from an external source, the patient may withdraw the part, or the whole body, as necessity indicates. If the stimulus arises from the internal environment of the body, it acts as a warning for the individual to seek relief, which he usually does by consulting his physician. Of course his past experience may play a part and he may try self-remedy before seeking professional help. This conscious evaluation of the internal pain introduces the problem of pain modified by past experience and will be discussed at greater length later.

Review of the literature

The physiology and neuroanatomy of these pain mechanisms were relatively simple up to the time of Sherrington. However, many experiences, including those of World War II and the Korean conflict, have taught keen, observant Armed Forces physicians that the older explanations must be modified to fit the observed facts relating to war wounds and pain. Since 1945, many papers have been published attempting to correlate physiologic, anatomic, and observed facts. These will be explored in their proper order.

Also since World War II, physicians are more acutely aware of the problem of the aging. The advent of medicine capable of prolonging human life, especially the life of the chronically ill, has created another problem—that these people have many and more vague complaints which are commonly termed

chronic pain. A large part of this problem stems from the lack of tools and methods for measuring pain. It is hoped that the present discussion will clarify the vagueness of such a term and show that chronic pain is more an experience than bona fide spike potentials indicating specific impulses along given peripheral nerves. The treatment thus must be directed to the origin and not to the projection of the experience.

Pain is a sensation which challenges definition, as the following quotations will illustrate. The Encyclopedia Americana describes it thus: "Pain, a sensation felt in animal bodies, always disagreeable and varying in degree from a slight uneasiness to intense agony."[1] Aring[2] states, "pain, then, is a phenomenon so elusive that authority is unanimous in telling us that it cannot be defined." Just previous to this quotation, he says, "there is no way to transmit the idea of the severity of pain short of experiencing it oneself." Sherrington[3] describes pain as being the psychic component of a protective reflex, and Walters[4] describes pain as having 3 components: (1) the pain sensation, which is the result of impulses set up by a painful stimulus traveling over peripheral pathways to the higher centers, where the impulses are modified as they are integrated and perceived in consciousness; (2) feeling tone, which is the unpleasantness accompanying the sensation and which may be felt apart from the sensation in anticipation or memory; and (3) the reaction to the pain, composed of reflexes and emotions. Pain, then, is a blend of these 3 components when they reach awareness. It is not a physical entity but a mental sensation, with unpleasant feelings and automatic responses. Rome[5] is more elaborate in his statement that chronic pain is corrosive—it dissolves fortitude and undermines ethics; its severity seems to become a function of its chronicity. The experience of pain welds body and mind. It exacerbates anxiety by its threat to organic integrity. Such varied definitions reveal only that pain is a phenomenon of unpleasantness and, later, even this will be disputed.

Physiology of pain

The neuroanatomy of the pathways as taught in medical school thirty years ago made the course of painful stimuli relatively easy to follow and remember. "There are good reasons for concluding that the fine fibers of the dorsal root, which enter the dorsolateral fasciculus of Lissauer and ultimately terminate in the substantia gelatinosa of Rolando, are primarily concerned with the conduction of nerve impulses resulting in pain, temperature sensations, and of course, with the associated reflexes."[6] The second order neurons cross rapidly through the ventral commissure to the lateral funiculus, where they ascend, forming the lateral spinothalamic fasciculus and associated spinotectal tract. The lateral spinothalamic fasciculus passes upward and continues to grow in size because of the addition of fibers to its medial border. In the region of the medulla, this tract joins with other tracts to become the spinal lemniscus, which terminates in the lateral thalamic nucleus. Thence, the sensation travels by radiation to the cerebral cortex, where the tracts terminate in the posterior central and adjacent gyri.

Visceral pain fibers accompany visceral nerves, many of which find their way along the autonomic pathways. However, when they reach the level of their developmental segment, the pain fibers proceed as did the somatic afferent pathways—through the dorsal roots to Lissauer's tract—and course with other

pain fibers to the lateral spinothalamic tract.

Referred pain may be leakage by close proximity to associated fibers. The spike potential may be of sufficient voltage to set up a local excitatory state in those associated fibers which then send impulses to the thalamus. These impulses cannot be analyzed and radiate to the conscious centers, giving the interpretation of a dislocated site for the origin of the pain.

Some interesting newer concepts have led to a broadening of our physiologic interpretation of the clinical findings. Gerard[7] advances a theory of an electronic beat of nerves with no inhibition. This feedback mechanism would explain the maintenance of chronic pain without a peripheral stimulus and, therefore, the inability of the physician to elicit the sensation by examination. The projection of this pain is accomplished by the cerebral cortex. Loss of inhibition of the impulses with the constant or intensified feedback may easily accentuate the cerebral interpretation of the pain. The Aδ and C fibers are still the main conduction pathways of pain sensation from the viscera or the somatic structures, and their course to the central nervous system is unchanged. The threshold for C fibers is about 100 times that of A fibers and there are perhaps 4 times as many, but their conduction rate is about one-tenth that of the Aδ fibers. This substantiates the double pain phenomenon.[8]

The first deviation occurs in the cord, for Gerard claims that the δ fibers run up the ipsilateral dorsal column, while the C fibers cross to the ventrolateral column. They can still be separately found in the midbrain. Thence, they pass to the thalamus and radiate to the somesthetic areas of the cortex. Some of the fibers leave the thalamus, passing to the reticular formation. The δ fibers represent the epicritic, or clearly felt and local, pain, while the C fibers represent the protopathic, or diffuse-background, type of pain. This latter is the type that causes suffering, as distinguished from the sharp, cutting type of pain.

There is much that cannot be specifically explained, such as the leakage around surgical lesions produced to cut the course of the fibers. The more ancient C fibers hold up the perpetuation of chronic pain as causalgias by physiologic inflammation. Continued and repeated protopathic inputs build up excitation in the central neurons by summation, irradiation, synchronous beating, and reverberations in closed loops with a fixation of a hyperactive state.

Melzack[9] lists 5 pathways which effect pain as a sensation: central gray matter, central tegmental tract, reticular formation, lateral spinothalamic tract, and lemniscal tract. As do many others, he believes that all pain is modified by past experiences.

Psychologic aspects of pain

The preceding material points clearly to the fact that pain is more a symptom than a physical sign. This must then involve the psychologic reactions to the perceived stimuli. Indeed, most of the recent literature refers more strongly to this aspect of pain than to definition of the specific neuroanatomic pathways. Beecher[10-12] relates his experiences during World War II, when about two-thirds of the severely wounded soldiers received at an aid station preferred a cigaret to morphine because they were not suffering from intolerable pain. To some of these soldiers, the wound was a pass out of the area of conflict and, perhaps, home. This may even have been a pleasurable situation for them

and, therefore, the pain was pleasant rather than hurtful.

The recent interest in the subjective phenomena of pain has cut across all sections of the field of medicine. Investigators[2-5, 10-17] have elaborated upon the psychogenic aspects of the pain experience. The child's response, when he has been injured, to his mother's kiss lends to the future experience of the child and modifies, as well as mollifies, his future responses to painful stimuli. The environment often influences the intensity and seriousness of the pain. Nearly everyone has experienced a toothache during the night. All external stimuli have been subdued, and this intensifies the mental reaction to the pain. The advent of morning, with renewed awareness of the surrounding world, reduces the severity of the toothache, and the approach to the dental appointment and chair induces sufficient apprehension to obviate most of the pain from the toothache.

Another aspect, psychologic in nature, is the pleasurable anticipation of the sequela of the pain. The child who receives motherly love after a spanking for a misdeed may well lead himself purposefully to other misdeeds to receive the love which will follow. This may lead to the masochistic desire for pain to reap the resulting benefits—"It feels so good when you stop."

The influence of deep concentration on some other activity may minimize or obviate pain. An example of such behavior is the athlete, so engrossed with his activity that he does not feel any particular sensation after a serious injury. He may even continue the activity to the detriment of his own health. The boxer is a good example of this type of response. Barber[18] goes even further when he states that "pain in the sense of discomfort and suffering is not necessarily present when noxious stimuli are discriminated, differentiated, and localized."

Rome[5] places the physician in the role of a crucial person. When the physician has been called to care for a patient's pain, the very thought that the doctor is on his way relieves the patient. Sometimes, as the physician approaches the bedside, the pain becomes worse—a fear for the result of his examination. Thus, the physician becomes a symbolic figure. Nothing less than the whole person is involved in the experience of pain.

Another facet of the psychogenic effect of pain is involved with personal security. The patient feels secure in the hospital, where his pain is relieved, his physical disabilities are treated, and he receives the personal attention of the aides, nurses, and doctors, who give him the confidence he needs to meet life. However, the recovery of the patient leads to the anticipation of discharge. This, in turn, leads to a chain reaction—the patient will be going home, where he will not receive attention to his personal problems; he will have to go back to a job he may not like and he must face the turmoil of life and its hardships. This leads to a searching appraisal of his internal physical and mental milieu. He cannot tolerate these unfavorable forces, and the symptom of pain returns. The proper hospital personnel are notified of this pain, and, soon, he is again receiving special attention. He becomes affixed to the protective environment of the hospital, and his hold on this favorable position is his pain. A summary of such a case, with serious complications, follows.

Case report

E.H., a 54-year-old woman, was admitted to hospital February 22, 1956, with vaginal discharge as her chief symptom. She had a nine-

year history of multiple sclerosis, which did not handicap her office work.

In October 1955, she fell, sustaining a fracture to the neck of the left femur. This was pinned and plated on November 6, 1955. She was transferred to a nursing home and, while awaiting recovery, developed the vaginitis.

The vulvovaginitis improved with conservative therapy. Roentgenographic examination of the left hip revealed absorption of the neck and necrosis of the head of the femur. The Jewett nail and plate were removed March 14, 1956. Recovery was uneventful, and the patient was sent to the convalescent section of the hospital for rehabilitation. She appeared to work very hard at physical therapy until it came time for her to walk alone, which she could do in the parallel bars. The motor manifestations of the multiple sclerosis involved only the lower extremities, evidenced by minor spasticity, and did not subjectively bother the patient.

However, after about one month's stay in the convalescent hospital, when it appeared that she would improve sufficiently to be discharged, she began to exhibit multiple symptoms, most of which could not be substantiated by physical examination or laboratory tests. A list of her complaints, as found in the progress notes of the chart, consists of: (1) April 5, 1956—multiple vague complaints, treated with aspirin; (2) May 15, 1956—pain in the joints of the wrist and hand, treated with aspirin; (3) September 5, 1956—pain in the left knee, roentgenogram subsequently showing osteoporosis of the knee, which, again, was controlled by aspirin; (4) February 25, 1957—pain in the left costovertebral angle; (5) March 2, 1957—pain in the left knee; (6) March 13, 1957—pain in the chest; (7) June 26, 1957—an ingrown toenail, with little pain, which was controlled by aspirin; (8) December 11, 1957—pain in the left shoulder and back; and (9) February 10, 1958—general muscle pains and headache. During the course of these chronic complaints of pain, the patient was put on a Darvon experiment and showed equivocal responses to the Darvon, placebo, aspirin, and codeine.

The psychologic pattern that the patient developed was noted early by the social service worker, therapists, doctors, and nurses working with her. Whenever a discussion of her discharge was approached, the patient had an exacerbation of pain in some area. She became emotionally unstable but, at the same time, proclaimed that she was doing well with her rehabilitation and that she would soon be independent.

There were several episodes of fever and, on January 9, 1957, hemorrhagic cystitis. When these events occurred, the chronic pain symptoms were never evident. On September 3, 1958, discharge back to the nursing home was discussed with the patient. She pleaded for one month more of rehabilitation, which was granted. On October 3, 1958, she asked for a further extension of her treatment because she was doing so well. This was followed by a downhill course in the patient's ability to concentrate on her efforts of rehabilitation. On October 21, 1958, she had a temperature of 102° F., became progressively worse, and, on November 5, 1958, began to vomit bright red blood. She was moved to the acute section of the hospital immediately, examined, transfused, and prepared for surgery.

Surgery revealed 5 gastric ulcers, one of which was hemorrhaging. A 75 per cent subtotal gastrectomy was performed. The patient seemed to have an uneventful recovery. During the first twelve postoperative days, the patient had a total of 18 doses of Demerol, 75 mg., for pain. The greatest number of doses in any day was 3. It was evident that pain was not her primary interest at this time, because security was, for the time being, assured. On November 30, the patient had a sudden episode of vomiting, at which time the examination revealed a mass in the right upper quadrant which was subsequently proved to be a perinephritic abscess. The patient was transferred to the genitourinary service, where she was treated conservatively until December 5, when several stones, one of which was obstructing at the ureteropelvic junction, were discovered in the right kidney. On December 15, 1958, she had an incision and drainage of the perinephritic abscess, with a nephrostomy. In spite of all treatment, septicemia developed with multiple embolic phenomena and she expired January 9, 1959. During the last two months of her life, chronic pain, or even acute pain, was very seldom mentioned by the patient. It seems evident that peripheral stimulation of pain endings leading to the patient's multiple complaints and the chronicity of the situation were certainly not in evidence.

There is no doubt that this patient had physical pain at several intervals during her long hospitalization. Where this pain passed through the spectrum of pain,[13] and perhaps reversed its direction, is not clearly defined, but she had all types of pain, which, in all probability, were the result of fear and insecurity. Was the physician perhaps a contributor to this poor patient's lot? Aring[2] uses the term empathy, in contrast to sympathy. This may be the weak point in the physician-patient relationship.

Control of pain

The patient who comes to the physician with the chief symptom of pain is demanding relief from the pain. It is then the duty of the physician to try to determine the cause of the pain and to remove it. For the acute, defensive type of pain, this is the usual course of events. In this situation, the law of cause and effect is the influential factor in solving the patient's problem. There are 3 general classes of treatment for pain—surgical, medical, and psychiatric.

Surgical treatment. MacCarty and Drake[19] list 7 surgical procedures for the control of pain: (1) posterior root section for trigeminal neuralgia; (2) section of the ninth cranial nerve for glossopharyngeal neuralgia; (3) posterior rhizotomy or neurectomy for other parts of the body (and the authors hasten to add that this procedure is of limited value); (4) spinothalamic tractotomy for thoracic and cervical levels; (5) lobotomy, gyrectomy, and topectomy, these procedures having limited value in the control of pain and possibly altering the patient's personality; (6) sympathectomy, in carefully selected cases; and (7) hypophysectomy, which has been beneficial, in some cases, for the pain of carcinoma.

Slaughter and associates[17] advocate palliative surgery for the relief of pain in cancer patients. They relieve the obstruction and pressure of large tumor masses by excision, which may be followed by palliative irradiation, chemotherapy, or endocrine modification where indicated. They also include sensory nerve blocks, neurosurgical procedures, and the use of pharmacologic agents for the control of pain. They believe that Thorazine is a good adjunct to other drugs. Thorazine acts similarly to lobotomy in dissociating the importance of the pain. With narcotics or analgesics, it affords satisfactory control of pain in many instances. Houde[20] agrees in general with these principles, adding psychotherapy to his armamentarium. Cleveland and Steiver[21] also have a list of surgical procedures for intractable pain.

The surgical treatment for pain is not a panacea, nor is it infallible. Burdick[16] defends nerve block because it has often been beneficial when other methods have failed. He believes that these methods have always been delayed in favor of conservative treatment. Perhaps this is the reason for so many failures. In defense of conservative measures is the fact that surgical measures are permanent, nonreversible, and not without some risk of complications, even under the best of conditions. If the pain is relieved by conservative measures, postponement of surgical methods seems to be justified.

The failures of the less radical surgical procedures center about the numerous pathways opened up to conduction in the central nervous system concomitant with persistent pain and chronicity. Engel[14] points out that "once the psychic organization, necessary for pain, has evolved, the experience—pain—no longer requires peripheral stimulation to be provoked." If this were the case, the minor procedures would be doomed to failure before they were undertaken.

The more radical procedures of lobotomy, gyrectomy, and topectomy are not measures to eradicate pain but rather to eliminate the constant consciousness of pain. Those patients who have had successful lobotomies can recall the sensation of pain at will but are no longer disturbed by it. Some authors believe that some of the drugs used have the same effect.

Medical treatment. If pain were a specific sensation and if a drug were

available which would prevent conduction in the nerve that carried the painful impulse, then there would be little need for any other drug for the control of pain. However, the text of this paper seems to imply that there is nothing consistent about pain and, therefore, the approach to drug therapy is an open field. To the pharmaceutical houses, this means an open market. The result has been a flooding of the market with proprietaries all reputed to offer the best control of pain.

Any standard pharmacology textbook discusses the properties of the pain-relieving drugs. "New and Non-Official Remedies" is published annually, enumerating the acceptable new drugs and evaluating their properties. From these sources, the effects of these drugs, supposedly influential in the control of pain, may be read. The race between pharmaceutical firms now is leveled toward drugs having narcotic properties for the control of pain without the side effects of narcotics.

The 2 main side effects they are trying to avoid are habituation and the need for observing the regulations of the Harrison Narcotic Act. Despite claims to the contrary, no firm has yet produced a drug that will replace the narcotics without finding that it, too, has the same undesirable side effects and immediately is placed in the category requiring regulation. The fact that the race is still on is evidence that the satisfactory drug has not yet been discovered.

The salicylates are probably the chief drugs used for the control of chronic pain. Smith[22] has recently written an excellent review on the pharmacology of the salicylates, in which he summarizes their effectiveness. As antipyretic agents, they increase heat loss by cutaneous vasodilation. As analgesics, the site of their action has not been finally determined; they may act centrally, but there is increasing evidence that they may reduce local edema. They have no antipyretic or analgesic effect on normal subjects.

The salicylates can easily be taken orally, are readily absorbed, and give relief in a short time. There is evidence that they irritate the gastric mucosa in some patients, but food, especially a small quantity of milk taken at the same time, reduces this irritation. In spite of TV advertising, there is no unequivocal evidence that combinations of antipyretics, analgesics, and central nervous system stimulants act synergistically.

More recent drugs, such as phenylbutazone, have been introduced on the market as being able to alleviate specific types of pain or suffering and may eventually prove to do so. However, their use for general chronic pain is unwarranted. This applies also to the group of corticosteroids and their many combinations. The untoward side effects of this latter group are severe enough to warrant extreme caution before prescribing the drugs.

Probably the most universally accepted group of drugs for the control of acute pain is the narcotics. Their action was generally considered to be that of raising the threshold to pain in the peripheral nerve endings. However, more recent evidence indicates that they act on the radiation elements from the thalamus to the cortex.[10,18] Melzack[9] points out that only 75 per cent of a series of postoperative cases received the benefits of pain relief from morphine, in spite of its general acceptance.

For chronic pain, codeine or codeine and aspirin are the only drugs used with any consistency, and there is some debate as to the effectiveness of this method of treatment. This has led to

the manufacture of many nonnarcotic drugs to be used in place of the codeine, either alone or in combination with aspirin. Carefully controlled double-blind clinical tests of these new compounds have not resulted in any startling results. Most authors find little to choose between the new drug and the aspirin or, in a percentage of cases, the inevitable placebo.

Beecher[12] probably has accumulated the greatest series of studies of the effects of placebos. In one series of 1,000 cases of all types of pain, he found 35.2 ± 2.2 per cent in which placebos were effective in the control of pain. Every physician has found cases in his own practice in which this is true. One should never underestimate the power of the placebo under the proper set of circumstances.

Psychiatric treatment. This leads to the final type of pain control, psychiatric. The greater evidence accumulated from the past fifteen years of experimental research in the field of pain indicates that the cortex of the brain is the final receptor and interpreter of this sensation. If this is a sound deduction, then psychiatric treatment is probably the most important of all methods. To be thoroughly oriented to the importance of this aspect of chronic pain, one should read the recent reviews by Aring,[2] Rome,[5] Gerard,[8] Melzack,[9] Cooper and Braceland,[13] and Engel.[14]

How does the physician practice the psychiatric treatment of chronic pain? First, he takes time to listen to the patient; often, the opportunity to express his feelings is sufficient to relieve the patient of the symptoms of pain. Second, he must show empathy[2] instead of sympathy for the patient's troubles. Third, he must thoroughly rule out a specific disease process, the treatment of which would relieve the pain; this is only accomplished by careful history taking and physical examination. Finally, he must treat the patient by whatever method he hopes will eliminate the pain symptoms; if this involves the use of the latest pain reliever—perhaps aspirin, placebo, or mental catharsis—it is justified if it works.

The physician must be careful not to fall into the trap of cause and effect. Did the patient get well from the action of the drug administered or in spite of it? Was the art of handling the case rather than the medication the successful therapeutic agent? The literature is filled with uncritical, uncontrolled enthusiasm for new drugs not of proved value, but, when the true story is known, the success resulted from the professional manner with which the physician handled the case. In this day of mass production and overloaded offices, too often the physician tends to be short with a patient. Also, the curt reply that the patient's difficulty is all in his head does irreparable damage, even though it may be true. To quote a final word of warning from Cooper and Braceland,[13] "hostility begets hostility. It is never permissible, in the practice of medicine, for the doctor to become angry at the patient who complains unduly."

Modern practice, with large patient loads, overwork, and other demands on the physician's time, may exceed the twenty-four hours in the day. How, then, can the physician care for the immediate needs of the ill and still carry out the treatment as discussed here? This is a question which cannot be answered, but if the ill are to be treated, then each patient must be considered as a whole man and the physician must give ample time to the evaluation of his problem. If all chronic pain were adequately treated the first time the symptoms appeared,

perhaps repeated visits for the same complaint would be eliminated.

Only a very few of these chronic pain patients will have to be referred to the psychiatrist. Another few may be helped by the psychologic support of a mental hygiene clinic, a psychologist, or both. A still smaller group may benefit from hypnosis.[18]

Summary

The problem of chronic pain is not similar to that of acute pain and cannot be treated by the same methods. The neuroanatomy and neurophysiology of the pain-carrying fibers cannot explain the complications involved in the clinically complex chronic pain. The patient's reaction to pain covers the spectrum from intense suffering to pleasure as experienced by the masochist or the patient who uses pain as a love object. The treatment or cure of chronic pain is not a simple matter of the choice of the right drug, since the whole patient and his past experience are involved in his symptoms. Perhaps the treatment of chronic pain in the geriatric patient is more difficult because he has had more experiences on which to base his symptoms.

One might say that success in the treatment of chronic pain in the geriatric patient is directly proportional to the ability of the physician to practice the art of medicine, an art which is based on his knowledge of the science of medicine.

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RALPH V. FORD, M.D.
Department of Medicine,
Baylor University, Houston

Treatment of hypertension with guanethidine and hydrochlorothiazide

Control of moderate to severe hypertension usually demands the administration of a diuretic agent and a more potent agent, such as guanethidine. Aside from the increased potency of such a combination, this regime has certain theoretic advantages over the diuretic Rauwolfia regime, mainly, decreased neuropsychiatric toxicity.

There have been many studies of the use of a diuretic alone[1] and the use of guanethidine alone[2] in the treatment of hypertension. Now the long-term (six months) effects of these agents, alone and in combination, have been observed, and these constitute the substance of this report.

Materials and methods

Fifty outpatients with hypertensive cardiovascular disease, ranging from moderate to severe, were the subjects of this study. The group consisted of 46 men and 4 women, whose ages were from 35 to 72 years. All previous medications used for the control of their hypertension were discontinued for three weeks or until the blood pressure had returned to its previous hypertensive level. The subjects were then divided into 2 groups: group I received hydrochlorothiazide (Esidrix) for three months, after which guanethidine (Ismelin) was added to the regimen for three months, and group II received guanethidine alone for three months and then guanethidine plus hydrochlorothiazide for three months. The dosage of the drugs was titrated according to individual decrease in upright blood pressure and severity of side effects. Observations on blood pressure, both recumbent and upright, side effects, and general clinical condition were made initially and at the following intervals: one, two, three, six, nine, twelve, thirteen, fifteen, eighteen, twenty-one, and twenty-four weeks.

Results

GROUP I

Hydrochlorothiazide alone (figure I). The average upright blood pressure in this group during the control phase was 190/120 mm. Hg (range 210/140 to 150/110). When hydrochlorothiazide, 50 mg. daily, was administered to the

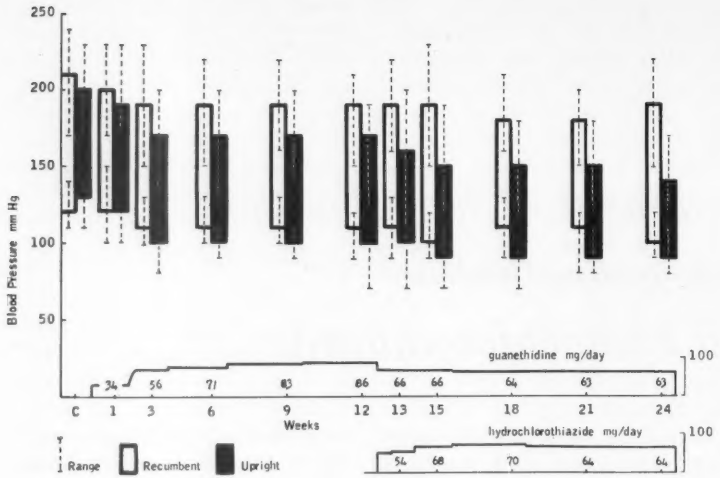

Fig. 1. Effect on blood pressure of hydrochlorothiazide alone and combined with guanethidine (average values, 25 patients). When hydrochlorothiazide is administered as the sole therapeutic agent, blood pressure decreases within one week. However, when guanethidine is added to the regimen, blood pressure decreases significantly within three weeks.

25 patients as the sole therapeutic agent, the average upright blood pressure at the end of one week was 180/110 (range 200/130 to 140/80). Although the average dose of hydrochlorothiazide was increased to 90 mg. daily (range 50 to 100) over the twelve weeks of therapy, the blood pressure did not decrease further. Side effects consisted chiefly of weakness but were not of such a degree as to be significant.

Hydrochlorothiazide plus guanethidine (figure I). When guanethidine was added to the pre-existing hydrochlorothiazide therapy, there was a slight additional decrease in upright blood pressure within three weeks (week 15) to an average of 160/100 (range 200/110 to 90/70). At this time, the average dose of guanethidine was 70 mg. daily (range 25 to 125 mg.), while the average daily dose of hydrochlorothiazide was 72 mg. (range 50 to 100 mg.). At the completion of twelve weeks' (week 24) therapy with the combined drugs, the average upright blood pressure was 150/90 (range 180/100 to 110/70), while the average daily dose of guanethidine was 73 mg. (range 25 to 125 mg.) and of hydrochlorothiazide, 76 mg. (range 50 to 100 mg.). Of the 25 patients, 8 noted side effects, such as weakness, diarrhea, dizziness, and inability to ejaculate, but these did not appear to be of significant degree.

GROUP II

Guanethidine alone (figure II). The average control upright blood pressure in this group was 200/130 mm. Hg. (range 230/130 to 190/110). After three weeks' therapy, upright blood pressure decreased significantly—to 170/100 (range 200/100 to 140/80). The average daily dose of guanethidine at this time was 71 mg. daily (range 50 to 100 mg.). After this, the upright blood pressure remained essentially unchanged, and, at the end

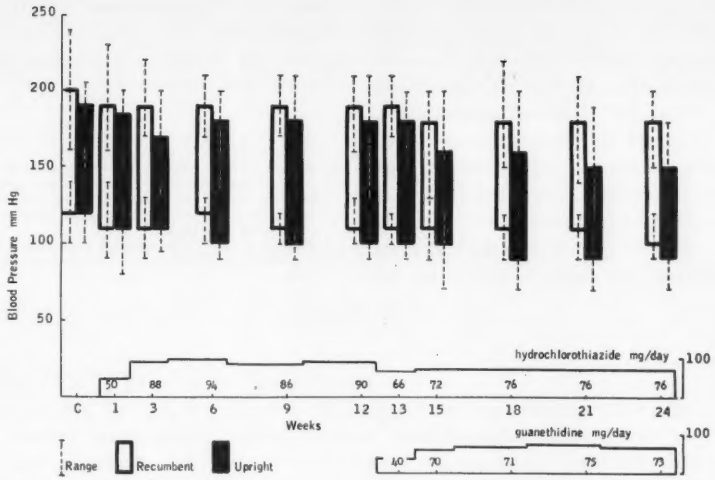

Fig. 11. Effect on blood pressure of guanethidine alone and combined with hydrochlorothiazide (average values, 25 patients). When guanethidine is administered as the sole therapeutic agent, blood pressure decreases significantly within three weeks. Addition of hydrochlorothiazide to the therapeutic regimen potentiates the effect of guanethidine, and blood pressure decreases further.

of twelve weeks' therapy, the average daily dose of guanethidine was 86 mg. daily (range 25 to 150 mg.). Side effects on this regimen consisted mostly of dizziness, diarrhea, and inability to ejaculate but were not severe enough to warrant discontinuance of therapy.

Guanethidine plus hydrochlorothiazide (figure II). When hydrochlorothiazide was added to the pre-existing guanethidine therapy, there was an additional decrease in upright blood pressure within three weeks (week 15) to 150/90 (range 190/100 to 120/80). The average daily dose of hydrochlorothiazide was 68 mg. (range 50 to 100) and of guanethidine, 66 mg. (range 25 to 100). At the completion of twelve weeks' (week 24) therapy with the combined drugs, the average upright blood pressure was 140/90 (range 170/110 to 120/80). The average daily dose of hydrochlorothiazide was 64 mg. (range 50 to 100), while that of guanethidine was 63 mg. (range 25 to 100 mg.). Side effects, in order of their frequency, were dizziness, weakness, inability to ejaculate, and diarrhea. These effects were not so severe that it was necessary to stop treatment, however.

Discussion

Although hypertension may be controlled with diuretics alone, there are still many patients with moderate to extreme hypertension who require more potent agents. In our opinion, if the diuretic agents fail to elicit a satisfactory hypotensive response, a Rauwolfia compound should be added to the therapeutic regimen. If there still is no satisfactory response, a sympatholytic agent such as guanethidine should be added. However, the data of this report indicate that perhaps, in the case of the more severe hypertensive patient, guanethidine may be added to the program without the use of Rauwolfia. Further-

more, guanethidine, especially when coupled with a diuretic, may produce less neuropsychiatric toxicity than certain Rauwolfia agents.[3] It should be noted that the dose of guanethidine must be carefully titrated to meet the individual patient's requirements and, further, if a diuretic is administered in conjunction with guanethidine, the clinician must be aware of the necessity of reducing the dose of the latter because of the "potentiation" effects of the diuretic agent.

Esidrex and Ismelin were supplied by Ciba Pharmaceutical Products Inc., Summit, N.J.

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EXCELLENT RESULTS can be obtained in over 75 per cent of geriatric patients with thrombophlebitis, varicose ulcers, or segmental venous thrombosis by intramuscular administration of trypsin. Patients over 60 years of age respond as well, although not as rapidly, as individuals under 60, and persistence in treatment is essential for the best outcome.

Injection of Parenzyme Aqueous, 0.5 cc., containing 2.5 mg. of trypsin, is made into the deltoid or gluteus muscles once daily when inflammation is acute and three times weekly thereafter. If lesions recur after cessation of treatment, maintenance with weekly or biweekly injections is necessary. Antibiotics are given during the acute phase, with physiotherapy as needed. Moderate locomotion is encouraged; standing for long periods is limited to prevent orthostatic venous congestion. Treatment is discontinued only if allergic reactions occur at the injection site.

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GEORGE M. HASS, M.D.
Division of Pathology,
Presbyterian–St. Luke's Hospital,
Chicago

Experimental inquiry into pathogenesis of human atheroarteriosclerosis

Experimental studies in animals lead to a better idea of the pathogenesis of human atheroarteriosclerosis and emphasize directions which might be followed to gain a more complete understanding of this disease.

▶ It is convenient to regard human atheroarteriosclerosis as a complex combination of structural changes in arterial walls.[1-3] The accumulation of atheromatous material, especially in the intima, represents one change which may be designated as atherosclerosis.[4] The degenerations of structure of the arterial wall represent another group of changes. The sequences which characterize each type of mural degeneration and the subsequent reactions of arterial mesenchyme represent a process which may be designated as arteriosclerosis. The common sequences and reactions allow a subdivision of arteriosclerosis into the following types: (1) mural degeneration with calcification and with or without mural mesenchymal activation and (2) mural degeneration without calcification and with or without mesenchymal activation. Most people of advanced age have variable combinations of atherosclerosis and arteriosclerosis, so that the term atheroarteriosclerosis may be used to refer to the combined disturbances. The principal untoward result of such combinations is to impair circulation of the blood and provide the soil for complications such as thrombosis and rupture with hemorrhage.

The principal purpose of this paper is to discuss the extent to which animal experimental studies have led to a better idea of the pathogenesis of the human disease and to emphasize directions which might be followed to gain a more complete understanding.

Relations between human and experimental atherosclerosis

These relations will be discussed from the point of view that human atheroarteriosclerosis is essentially a disorder with a single pathogenesis, namely, hyperlipemic hypercholesteremia. From an experimental viewpoint, the problem, therefore, is approached by the produc-

tion of hyperlipemic hypercholesteremia in one or more animal species.[4-9] The experimental disease may then be compared with the human disease.[5,10] It is certain that the human disease usually increases with age, probably not because susceptibility increases with increasing age but because of the duration of a slowly rising average level of hyperlipemic hypercholesteremia.[11] Experimental evidence indicates that this interpretation is probable because the age of the experimental animal has much less to do with the rate of development or severity of the vascular disease than do the duration and level of hyperlipemic hypercholesteremia.[12]

At a sufficient level of hyperlipemic hypercholesteremia maintained for a sufficient time, a pattern of atherosclerosis develops in the experimental animal. This pattern is essentially the same in all species and is accurately reproducible in individuals of the same species.[6,10] Usually, the magnitude of the disease is maximal in the proximal aorta and decreases distally in some larger branches. In other branches, it increases distally; it may be quite severe in small arteries and arterioles of some organs while other organ systems are spared. Meanwhile, xanthomatous accumulations ordinarily occur in many extravascular cells and tissues, as well as in the reticuloendothelial system. This occurs long before there is any significant disease in many large arteries regularly affected in man. However, it is also generally true in man that the xanthomatous disease of peripheral arteries decreases in the direction of blood flow as arteries decrease in caliber and becomes insignificant in arteries within parenchymatous organs. Without discussing further details, it is clear that the pattern of the common forms of atherosclerosis in man is different from the pattern produced in animals by hyperlipemic hypercholesteremia.[5,10]

Though the over-all pattern of distribution in man and animal may differ, the initial xanthomatous deposits in the intima and the local mesenchymal reaction to these deposits closely resemble one another. These deposits appear as small plaques which increase in breadth and thickness. They tend to become confluent, and their thickness seldom greatly exceeds the thickness of the subjacent vascular wall. In the experimental animal, the location of the plaques is surprisingly uniform among members of the species. In man, however, the position of atheromatous plaques varies widely from person to person, so that there is only a superficial resemblance to a common pattern.

In man, the intimal xanthomatous plaques generally undergo a sequence of developmental and subsequent deteriorative changes. In early stages, they are composed principally of lipid-laden mesenchymal cells, or foam cells, between which is a modest accumulation of intercellular material rich in various lipids. Though these cells may have a variable life span, they tend to undergo degeneration and lysis, with liberation of accumulated lipids into the interstitial environment. Doubtless, some of the liberated material is resorbed or transferred to other mesenchymal cells in the area, but much of it remains, with modifications leading to crystallization or mineralization through the attraction and fixation of calcium salts. These sequences occur in much the same way in uncomplicated experimental hyperlipemic hypercholesteremic disease. As they proceed in all species, there is commonly an involvement of the media of arteries characterized by an indolent accumulation of lipids. In man, however, the deteriorative changes often are ei-

ther preceded or followed by conspicuous mesenchymal activation, with fibrogenesis, vascularization, and medial degeneration of a fibrocalcific type. These changes are inconspicuous or absent in uncomplicated experimental hypercholesteremic disease and, for these events to acquire prominence in the experimental disturbance, the soil must be prepared by conditions other than hyperlipemic hypercholesteremia. In general, these conditions produce medial degeneration and elicit mesenchymal activation in the arterial wall.[1-3, 10, 12, 13] Deterioration of xanthomatous intimal plaques in hypercholesteremic disease inhibits fibrogenesis by activated mesenchyme, fails to stimulate vascularization of plaques, and is not productive of medial disease comparable to that commonly encountered in human atherosclerosis.[10, 12]

In man, it is generally conceded that a level of blood pressure sufficiently in excess of that which the vessel is designed to withstand increases the probability of intimal xanthomatous accumulation.[1] There is no proof that this is the case in hypercholesteremic disease of animals. It may be that the observed effects in man, especially those occurring in the pulmonary arteries in patients with mitral stenosis or in veins subjected to excessive pressure, are not attributable to pressure alone but rather to the activation of intimal mesenchymal reactions favorable to lipid accumulation. It is possible that organization of mural thrombi plays a role in this connection.

In man, it is also generally conceded that the probability of occurrence of intimal xanthomatous disease is increased in the presence of hypercholesteremia and that the rate of development and degree of the disease tend to increase in proportion to the level and duration of hypercholesteremia.[11] This is certainly true in most experimental animals. The lower limits of the required level in man, however, are at least as low as normal adult levels, because excessive disease commonly occurs in people with blood cholesterol levels between 180 and 250 mg. per cent. With induced levels of this magnitude in otherwise healthy animals, it is practically impossible to produce significant atherosclerosis. Indeed, in animals, it is generally necessary to maintain levels in excess of 350 mg. per cent over long periods in order to obtain even a modest degree of experimental atherosclerosis in a normal arterial system.[6, 7, 10, 12] Such levels are seldom found in man. Therefore, from an experimental viewpoint, the conclusion is drawn that something more than the usual level of blood cholesterol is required for the development of significant intimal atheromatous disease in man. If the "something more" is related to composition rather than to the level of lipids and cholesterol in the blood, the required composition has not been produced experimentally. If it is related to duration in terms of decades, this remains for analysis in animals with very long life spans.[13-15]

There are, however, some conditions in man in which hyperlipemic hypercholesteremia is excessive and prolonged, such as familial hypercholesteremia, Schüller-Christian disease, nephrosis, and hypothyroidism. In these diseases, there is a tendency for general xanthomatosus to develop, as it does in experimental animals with similar blood cholesterol levels. There seems, however, to be no unexpected accelerated development of atheroarteriosclerosis in these cases, such as is common, for instance, in patients with diabetes mellitus uncomplicated by high blood lipid and cholesterol values.

In man and experimental animals, the earliest significant effect of intimal atheromatous deposits is encroachment upon the vascular lumen. This produces no easily recognizable effects on the integrity of most organs in the experimental animal, although myocardial infarcts occasionally occur. This is surprising, because the degree of arterial stenosis is often extreme. It seems, therefore, that something more than arterial stenosis caused by severe intimal atheromatous disease is required for the development of many changes in organs and tissues ordinarily attributed to circulatory insufficiency in man. Similarly, other complications, such as aneurysms and arterial rupture with hemorrhage, so common in man, have not been encountered experimentally. It is clear, therefore, that the common complications of human atheroarteriosclerosis rarely occur in animals with extreme degrees of general disease secondary to severe hyperlipemic hypercholesteremia. Absence of these complications may be attributed to a difference in the local degenerative and reparative sequences in arterial walls of man and animal. In the experimental animal, atheromatous plaques degenerate but do not ulcerate or accumulate much calcium. In man, atheromatous plaques commonly degenerate, ulcerate, and acquire considerable calcium before ulceration. In the experimental animal, the degeneration of atheromatous plaques does not elicit significant ingrowth of vascularized granulation tissue, while in man this is common.[16]

Finally, in the experimental animal, the development of occlusive or even easily recognizable minute mural fibrinous thrombi overlying degenerate atheromatous plaques never occurs in some species and only seldom occurs in others.[10, 15, 17] Therefore, in man, something more than is easily produced by hyperlipemic hypercholesteremia in animals is required for the development of fibrinous thrombi over atheromatous lesions. Experimental evidence indicates that the "something more" is derived from the capillary bed which forms in the repair of degenerate atheromatous lesions in man and fails to form in most animals.[16]

Relations between human and experimental arteriosclerosis

In man, there is a degenerative and reparative arterial disease which begins in early life, proceeds slowly until about the fourth decade, and, thereafter, progresses more rapidly in some persons than others, especially in the fourth, fifth, and sixth decades. This disease (1) is characterized principally by chronic progressive medial deterioration with or without calcification or significant mural mesenchymal proliferative reactions; (2) tends to produce dilation, elongation, and tortuosity of vessels, with variations leading to decrease in caliber in the presence of sufficient intimal proliferative reactions of fibrocellular nature; (3) affects different parts of the arterial system to different degrees in the same individual and has a variable pattern of distribution and severity in different people; and (4) seems to begin with deterioration of medial structure. This deterioration is usually accompanied by a variable accumulation of calcium salts and a variable activation of mesenchyme, with resorptive, reparative, proliferative, and fibrogenic sequences. Most experimental animals do not, as they grow older, develop a conspicuous disease of this type. Furthermore, there is no satisfactory experimental reproduction of this human disease. It is possible, however, to reproduce many of the histopathologic features of the disease by administration

of excessive amounts of vitamin D to experimental animals.[10, 13, 18-26] Other degenerative calcific medial disorders may be produced by local hypothermia,[2, 12] lathyrism,[27] hyperparathyroidism,[28, 29] renal insufficiency,[30, 31] pyridoxine deficiency,[32] and magnesium deficiency.[33] Among these, hypervitaminosis D has advantages from an experimental viewpoint because of the ease with which the disorder can be controlled and accurately reproduced in acute or chronic form in several species.[34]

In rabbits, hypervitaminosis D is characterized by a calcific medial degeneration with mesenchymal reactive sequences which closely resemble those occurring in human senile calcific medial disease.[24] The pattern of distribution of the disease in the animal, however, is different from that of senile human calcific disease, especially in certain peripheral arterial systems. In the aorta and its major branches, the patterns are essentially similar. There is a wave of medial degeneration, with calcification beginning in the proximal aorta and progressing distally into the major branches. This begins with focal lesions in the inner media. As these enlarge in the longitudinal and circumferential directions, they become confluent and eventually involve the full thickness of the media. Accompanying this process is a variable activation of mesenchyme, which, in the intima, leads to fibrocellular thickening that tends to approximate the thickness of the subjacent wall of larger arteries. In the media, fibrocellular reactions develop and, as vascularized stroma penetrates from the adventitia, resorption of the calcified media proceeds with increasing rapidity, resulting at times in replacement of the entire media with granulation tissue. At other times, bone is formed as vascularized resorption of the calcified structures progresses. These events closely resemble those commonly found in the aorta and large muscular or musculoelastic arteries in human arteriosclerosis. As time passes, secondary changes of a calcific degenerative nature may appear in the regenerated intima which, as it matures, often acquires elastic fibrils and smooth muscle cells. Occasionally, xanthomatous deposits accumulate in the intima and media as these lesions develop, but such accumulations are never conspicuous unless the blood cholesterol levels, usually increased by excessive vitamin D dosage, rise from the normal of 60 to 80 mg. per cent to about 150 to 250 mg. per cent.[10, 13] Xanthomatous deposits under these conditions are restricted to areas, especially the intima, in which mesenchymal proliferation is most active and are not encountered in adjacent normal or abnormal intima composed of newly formed thick layers of dense mature fibrocellular mesenchyme. These observations indicate that combinations of hypervitaminosis D and hyperlipemic hypercholesteremia might provide experimental conditions suitable for reproducing disease similar to human atheroarteriosclerosis.

Relations between human and experimental atheroarteriosclerosis

In order to obtain a satisfactory experimental reproduction of human atheroarteriosclerosis in its common form, there are several requirements: (1) xanthomatous deposits must accumulate in significant amounts in the intima at blood cholesterol levels similar to those in man; (2) calcium salts must accumulate in the media of the arteries of certain parts of the system; (3) mesenchymal activation in the media and intima must be excited in the reparative and resorptive sequences; (4) as a part

of these sequences, after degenerative changes, vascularization must occur in the media and abnormal intima; (5) fibrinous thrombi must form over the abnormal intimal lesions, especially in those arteries customarily affected by vascularized medial calcific and intimal atheromatous disease; and (6) the pattern of distribution of the disease must be subject to variation, so as to simulate the variable patterns encountered in man.

The key to the provision of the first requirement is intimal mesenchymal activation. This may be elicited in several ways, the majority of which involve injury and reaction to injury of the mesenchyme of the intima or subjacent media.[1,2,5] Indeed, there are reasons for believing that an interstitial infiltration and fixation of lipids represents a form of injury which elicits the mesenchymal reaction responsible for the primary xanthomatous intimal plaque in animals with hyperlipemic hypercholesteremia. The mesenchymal activation, however, must be qualitatively and quantitatively sufficient to so lower the threshold that lipid localization and accumulation may be induced at levels much below those required by normal intima with no activation other than hyperlipemic hypercholesteremia. In the experimental activations, this is realizable at cholesterol levels of about 180 to 250 mg. per cent.[10,13,17] The rapidity and magnitude of lipid localization at this low level under optimal conditions is often impressive.[10] Significant lipid accumulations in activated intimal mesenchyme may occur in a few days rather than the many weeks or months customarily required of normal intima in animals with very high blood cholesterol levels. That a similar rapid localization may also occur in man under optimal conditions of mural mesenchymal activation has also been demonstrated.[35] Intramural senile uterine arteries regularly show medial degenerative and fibrocellular intimal proliferative reactions but no atheromatous lesions. After intracavitary irradiation, there is often extensive atheromatous accumulation in the proliferating intima of the arteries affected by the radiation even though the blood cholesterol values are normal.[36] This usually occurs within three months. There is no reason for doubting that rapid localization of lipids may occur in arteries elsewhere in man under optimal conditions. The likelihood of such an occurrence is presumably increased in proportion to the level of blood cholesterol; the duration of the level; and the duration, nature, and location of the mesenchymal activation.

An appropriate understanding of these matters is based upon certain experimental observations. The first observation is that each part of the arterial system has its own characteristic threshold of resistance to the effects of a given level of blood cholesterol or a given dosage of vitamin D over a given time interval.[10,37] The pattern of intimal lipoidosis or medial calcification in the presence of hyperlipemic hypercholesteremia or hypervitaminosis D is ordinarily determined thereby in an otherwise normal arterial system.[10]

The second observation is that each part of the arterial system has its own characteristic threshold of resistance and form of reaction to a given injury over a given time interval. The probability of lipid localization or medial calcific degeneration at a given cholesterol level or dosage of vitamin D over a given time interval depends, therefore, not only upon the natural threshold of a given vascular segment but also upon the lowering or increasing of this threshold by those factors which govern the

threshold of resistance to injury and the form of reaction to injury over a given time interval.

The third observation is that the probability of lipid localization or medial calcific degeneration in a given vascular segment is increased if other vascular segments with lower thresholds have had their thresholds satisfied by lipid accumulation or mineralization or increased by other factors. In other words, the circulating plasma lipids and calcium salts have a tendency to accumulate in loci with the lowest thresholds, but if these loci are occupied or their thresholds are otherwise raised, lipid or calcium tends to accumulate in the location with the next lowest threshold.[10]

If these observations are valid, it is desirable to inquire into the synergistic and antagonistic influences by which lipid localization, calcific medial degeneration, and mesenchymal activation lead to variations in the pattern of atheroarteriosclerosis. If lipid localization is produced in a normal vascular system by dietary hyperlipemic hypercholesteremia and if, thereafter, in the same animal, hypervitaminosis D is produced, the pattern of medial calcific degeneration departs from that found in an otherwise normal animal. There is a pronounced tendency for the intimal lipid plaques to protect the subjacent media against mineralization, and the magnitude of the protection is roughly proportional to the thickness of the intimal plaque.[10,21] At the same time, calcific medial degeneration tends to be more severe in those parts of the system free from intimal lipoidosis.

In a second experiment, if calcific medial degeneration is produced in an otherwise normal vascular system by hypervitaminosis D and, thereafter, dietary hyperlipemic hypercholesteremia is established, the pattern of lipid deposition departs from that found in an otherwise normal animal. The modification of the pattern depends principally upon the state of mesenchymal activation incidental to medial calcific degeneration.[10] Lipid deposition tends to occur most readily in those locations, whether in the intima or media, in which mesenchymal activation is most vigorous and immature.[17] Lipid deposition tends to occur least readily in those locations in which the wall of the artery is solidly calcified and mesenchymal activation is minimal or in which activated mesenchyma is mature, healthy, and fibrous or resting. In this latter instance, there is a greater tendency for lipids to accumulate in the nearby normal intima than in the newly formed, thick, fibrous intima overlying areas of dense, calcific, medial degeneration.

In a third experiment, if dietary hyperlipemic hypercholesteremia and hypervitaminosis D are produced simultaneously, another pattern of atheroarteriosclerosis, which varies with the severity and duration of each provocative disorder, is formed. Under optimal conditions, conspicuous lipid localization occurs in relation to activated intimal and medial mesenchyme at cholesterol levels in the normal adult human range. At times, the arteriopathy closely resembles that customarily found in man and occurs in the absence of significant reticuloendothelial lipoidosis or extravascular calcium deposition in the parenchymal tissues.[10] However, there is never any evidence of thrombosis, despite severe vascularized medial calcific disease, prominent fibrocellular intimal proliferation, and conspicuous degeneration of large fibroxanthomatous intimal plaques infiltrated with calcium salts. Two events commonly found in man, namely, ulceration and vascularization of intimal lesions, are not en-

countered, emphasizing the possible contribution of these factors to thrombosis in man.[16]

Role of potentials in pathogenesis of atheroarteriosclerosis

The evidence indicates that each part of the arterial system has its own characteristic level of susceptibility, resistance, and reactivity to factors implicated in the pathogenesis of atheroarteriosclerosis. These levels may be defined as potentials.[10] Normally, therefore, the lipoidosis potential of each part of the arterial system determines the pattern of lipoidosis which develops in the course of a particular level of hyperlipemic hypercholesteremia over a particular time interval. Inherent in this concept is the thought that, as sites with highest potentials become replete with lipids, the probability of lipids localizing at sites with lower potentials is increased. Factors which determine the potential of each point in the system are obscure. Some relate these factors to permeability of the endothelium to serum lipids, to excessive pinocytic activity of endothelium for interstitial lipids, and to undue trapping of filtered lipids in the interstitial areas.[38] Others regard the problem as wholly related to metabolic lipid contributions by the cells locally rather than to serum lipid derivation. Still others emphasize the importance of the relation between the local circulatory forces and the capacity of the arterial wall to deal successfully with them.[1] Perhaps all of these factors are involved, each contributing in its own way to the basic lesion, which is an accumulation of lipid-laden, immature, mesenchymal cells derived from fibroblasts and endothelium. However one might wish to emphasize one or another theory, there is a certain inescapable fact, namely, the dependence of the occurrence of a lesion upon hyperlipemic hypercholesteremia, mesenchymal activation, or both.

The tendency for an arterial wall to undergo degeneration and calcification may be defined as a calcific degeneration potential. This is not necessarily the same as a degeneration potential or even a calcification potential, for relations between degeneration and calcification depend upon pathogenetic mechanisms. In the usual form of arteriosclerosis in man, the common association of medial degeneration and calcification in the larger systemic arterial systems cannot be denied. The association is not so apparent in the small branches of these systems, especially those in the parenchymatous organs. Here, the medial degenerative changes are usually not complicated by conspicuous accumulations of calcium. Thus, there is often a sharp transition between an artery with a high calcific degeneration potential and a branch with a very low or negligible one. There is no ready explanation for this in terms of structural or functional differences. Hence, it is convenient to postulate that each part of the arterial system has its own characteristic potential and to design experiments to study the problem.

One way to study the problem is to produce experimental conditions leading to calcific medial degeneration, which may be done in several ways. One method involves producing local medial degeneration and subsequent accumulation of calcium. If this is done by local freezing of the intact arterial walls, the evidence indicates that there is a variation in their susceptibility to calcification. Vessels such as the aorta promptly calcify, while other arteries known to be resistant to calcific degeneration fail to calcify, even though they are transmurally devitalized by the low temperature.[12]

Another way to study the matter is

to produce systemic disturbances characterized by general calcific medial degeneration, such as hypervitaminosis D. Analysis of the effects of this condition indicates that most species susceptible to the disturbance develop a similar pattern of calcific medial degeneration. This is a mysterious pattern which displays a ready susceptibility of some arterial systems and a total resistance of others.[37] This pattern seems to be governed not by structural similarities or differences but by some sort of coordination that leads to a high calcific degeneration potential in the media of arteries which supply parenchymatous systems which likewise have a high calcific degeneration potential. The nature of this coordination is unclear, but it seems that the arterial wall, in its development, may have acquired some of the elementary properties of the organ supplied by it. It is perhaps permissible to speculate that a similar coordination may bear upon the simultaneous development of pathologic changes in certain organs and the arterial systems which nourish them. After all, the structure which represents a capillary gradient at one stage of development may differentiate into an arterial gradient at a later stage, perhaps without losing all of its original properties.

Whatever the answer may be, there is no doubt that minute details of calcific medial degeneration, as it occurs in man in certain arterial systems, may be produced in animals with hypervitaminosis D and that this may occur without major increases in the levels of calcium or phosphate in the serum.[37] Furthermore, once the degenerative changes have occurred, reparative and resorptive events identical with those encountered in man ensue despite continuation of the state of hypervitaminosis D responsible for the calcific degenerative changes. It is apparent that the same situation occurs in the common form of medial calcific degeneration in man, because deposition and resorption of calcium often occur simultaneously, even in the same segment of an arterial wall. This likewise occurs regularly without any change in levels of calcium and phosphate in the serum. Similarities in observations do not necessarily imply similarities in pathogenesis, but it would be unwise to disregard the possibility that similar mechanisms are involved.

If the pattern of the disease in man were as constant as the experimental patterns, the problem would be simpler. As matters stand, however, the pattern in man is constant only in a semiqualitative sense. In any large group of aged patients, predictions of the magnitude and exact distribution of calcific medial degenerative disease are seldom confirmed at autopsy. Also, if the degree of disease in one arterial system is about the same in a series of patients, the probability that other arterial systems will have comparable involvement is small. In other words, if the degree of medial calcific degeneration of the aorta is known, this allows little basis for an accurate prediction of the degree of medial calcific degeneration of the coronary, cerebral, tibial, mesenteric, or other systems. Therefore, even though the medial calcific degeneration potential of each comparable arterial system of all people may be the same, the factors in different people which raise or lower the natural potential of a given system must be different in quality or quantity.

Role of mesenchymal activation potential

The mesenchymal, structural, proliferative reactions in the arterial wall reflect the mesenchymal activation potential.

These reactions may be excited by 2 important influences: (1) injury to the arterial wall and (2) change in circulatory dynamics. The capacity of the arterial wall to react to injury is not everywhere the same, and the nature of the reaction depends to some extent on the nature of the injury. In general, however, the patterns of the different reactions have much in common. The capacity of the normal arterial wall to react to a change in circulatory dynamics is also not everywhere the same, and the nature of the reaction depends to some extent on the nature of the change in dynamics. In general, however, the reactive pattern has some features in common with the pattern characteristic of the reaction to injury. For purposes of discussion, the view may be taken that the trend and result of these reactions are to secure the best possible adaptation to circulatory demands. This adaptation is almost perfect when the normal arterial wall is confronted with an increased circulatory demand. The artery grows, and its growth in some instances is very rapid, with substantial proliferation of all its structural components. The adaptation is also very effective when the normal arterial wall is confronted with a decreased circulatory demand. The artery undergoes atrophic changes, especially in the medial muscular elements, while the caliber of the lumen is reduced by fibrocellular intimal proliferation. Such reactions to circulatory demand are generally regarded as physiologic, but they are an accurate reflection of mesenchymal activation potentials and are important in pathologic conditions. Inasmuch as these reactive capacities are not necessarily retained by abnormal arterial walls, it is clear that the normal adaptations to changes in peripheral demand may be, depending on conditions, greater or less than expected. This is a matter of greatest importance in the accommodation of a rigid or partly occluded artery to its customary circulatory demand or to a different demand imposed by events such as progressive cardiac hypertrophy or local inactivation of segments of the kidney. This is also an important limiting factor in the enlargement of arteries required for the development of collateral circulations.

Of still greater significance are the mesenchymal reactions to injury. In general, arteries of similar structure and size have similar capacities. The simplest form of reaction involves intimal endothelial activation. With a given stimulus, this varies from place to place. It may be manifest by nothing more than swelling of endothelial cells, some being more responsive than others. It may be more complicated and involve an increased cellular activity as defined by pino- and phagocytosis of microscopic or ultramicroscopic substances in contact with the cell. This degree of activation is often accompanied by proliferation of the endothelial cells and subjacent fibroblasts, with a tendency for these cells to form a plaque. Under appropriate conditions, these plaques enlarge and fibrogenesis becomes conspicuous. With increasing age, the cellularity of the plaque ordinarily diminishes as collagen and elastic tissue appear in larger amounts. In time, these fibrils tend to assume an orderly orientation, and, between them, the mesenchymal cells may acquire the properties of smooth muscle cells..

It is a matter of interest that the qualitative and quantitative aspects of these mesenchymal reactions are determined by many factors, the most important being the particular arterial segment which is reacting. Ordinarily, the thickness of the plaque seldom exceeds the thickness of the subjacent arterial wall.

When it does exceed this thickness, a part of the thickness of the plaque has either undergone deterioration or acquired a blood supply. Therefore, as the sizes of arteries decrease, the magnitude of the intimal mesenchymal reactions is correspondingly decreased, so that the reaction may be negligible as small arteries become arterioles and these in turn become capillaries. Often, the composition of the proliferated intima tends to reduplicate, in an abortive and imperfect way, the composition of the subjacent arterial wall. This is more easily detected in the experimental animal, in which, for instance, alternate lamella of collagen and elastic tissue tend to form as the proliferated mesenchyme matures. Under similar conditions, maturation of the proliferated intima of the iliac and femoral or renal arteries tends to result in formation of smooth muscle cells between bands of collagen.

These mesenchymal reactions are governed by complex influences, bear little relation to the quantity of change in the arterial wall, bear a closer relation to the nature and discontinuity of the changes, and tend to be more conspicuous when the changes are close to the intima and at points where medial deterioration approximates well-preserved medial structure. This is demonstrated by experiments which involve local transverse devitalization of the media by hypothermia or hypervitaminosis D. The significance of medial deterioration cannot be discounted, as is illustrated by the sequences which develop in calcific medial degeneration, which ordinarily has a well-defined pattern in man. It is best recognized in patients who live to an advanced age without occurrence of severe atherosclerosis, which, as will be discussed later, modifies the pattern. A similar pattern is reproducible in animals with hypervitaminosis D if there is an appropriate combination of this disorder with a modest dietary hypercholesteremia. In each species, the similarities between the local lesions as they occur in many but not all arterial systems are impressive. The earliest sign of disease is in the inner media, where there are degenerative local structural changes which precede or accompany the accumulation of calcium. This process tends to spread circumferentially, in depth and in the long axis of the vessel, to establish continuity with similar local processes. As the medial calcific degenerative process approaches the vasa vasorum or the adventitia, a mesenchymal reaction is often excited and granulation tissue impinges upon the calcified structure. As this occurs, resorption of the calcified structure begins and continues as the vascularized mesenchyme becomes more abundant, slowly excavating the abnormal media until finally it may be removed entirely. This process also often leads to the local formation of bone.

This is the most active resorptive and reparative mechanism. Less active mechanisms seem to depend upon local cellular activity or the slow dissolution of calcified matrices in the absence of vascularized mesenchymal penetration. However this may be, calcium deposition and calcium resorption frequently occur simultaneously in the same vascular segment. It is significant that the medial resorptive reactions are usually governed by the invasion of vascularized mesenchyma that is usually traced to the adventitia or to arterial branches at their origin from the affected vessel. The origin of vascularized mesenchyma from the intimal aspect of the affected artery has not been as satisfactorily demonstrated in animals as in man. In our studies, the proliferated intimal mesenchyme has invariably remained avascular

and unduly resistant to penetration of richly vascularized mesenchyme, even though it has excavated and replaced the entire media. In man, the sequence of events is similar to that in animals, though vascularized mesenchyme at times may originate from the intima.[16] There are several reasons for emphasizing this aspect of the mesenchymal activation potential, the most important of which is the fact that fibrinous thrombi tend to develop frequently on degenerate vascularized intimal lesions and infrequently on avascular lesions.

Role of thrombosis potential

We have been unable to define the thrombosis potential of different arterial systems in the experimental animal. Thrombi often form where arterial walls are severed or structural continuity is otherwise interrupted. However, if structural continuity is not disturbed, the entire wall of an artery may be devitalized, by methods such as those involving low temperature, without the development of conspicuous fibrinous thrombi. Also, extreme degrees of experimental atherosclerosis, sufficient to occlude arteries and to lead to infarcts of such organs as the heart and kidneys, seldom lead to primary local fibrinous thrombosis. Indeed, such thrombotic complications have not been encountered by us at all in rabbits. In monkeys, fibrinous thrombi occasionally occur as a complication of severe chronic atherosclerosis.[15] The formation of fibrinous thrombi has not been observed by us in rabbits or other animals with hypervitaminosis D despite the occurrence of severe medial calcific and intimal proliferative disease, nor has the superimposition on this process of severe atheromatous disease in rabbits increased the probability of formation of fibrinous thrombi, so common in man in the presence of similar types of arterial disease.

The failure of experiment to aid in the definition of the susceptibility of different arterial systems to thrombosis requires an analysis of the relation between the tendency to thrombosis and the presence of atheroarteriosclerosis in man. When the analysis is made, it becomes clear that most local fibrinous thrombi occur in those parts of the arterial system which are characteristically involved by calcific medial degeneration and fibroatheromatous intimal disease. Arteries affected by calcific medial degeneration with or without fibrocellular intimal proliferation are not favorable sites for local fibrinous thrombosis. Arteries affected by atherosclerosis in the absence of calcific medial degeneration are also not sites of election for local thrombosis. Arteries affected by diverse medial degenerative changes with or without fibrocellular intimal reactions are not particularly susceptible to thrombosis. Inasmuch as the combination of calcific medial degeneration and fibroatheromatous intimal disease offers the best soil for thrombosis, arterial systems so affected may be regarded as having the highest thrombosis potentials, while arterial systems not so affected may be regarded as having low or negligible potentials. In a further analysis of this situation, the relative potentials would seem to depend upon the magnitude and nature of the local process. Among the local factors, degenerative changes in fibroatheromatous plaques seem important. This is especially so if the degenerative changes occur in vascularized plaques, increasing thereby the likelihood of intramural hemorrhage with complications.[16] The aorta, especially in the abdominal segment, is most susceptible to local processes which favor thrombosis. Therefore, it has, perhaps, the

highest thrombosis potential, and if we had the opportunity to observe the frequency of mural thrombosis, this would probably be confirmed. Fortunately, these are usually not occlusive thrombi and most are harmless, though they may serve as sources for emboli in narrowed arteries of the legs.

Other systems with high thrombosis potentials are the coronary, tibial, and cerebral systems. In each instance, the mural thrombotic process is initiated only in that part of each system affected by the processes emphasized previously. It would seem that the frequency of involvement of each system is roughly proportional to the degree of involvement by the processes but not necessarily proportional to the clinical or pathologic observations based upon the effects of arterial occlusion, for fibrinous thrombosis doubtless occurs commonly without producing arterial occlusion or significant symptoms. In the smaller arterial channels, this is perhaps most common in the anterior or posterior tibial arteries. The frequency of formation and lysis of nonocclusive fibrinous mural thrombi is probably much greater than is recognized in other systems, but, in the main, the predisposing factors would seem to be as stated.

Interrelation of arterial potentials

The lipoidosis potential of normal arteries is a reflection of their susceptibility to xanthomatous deposits, principally in the intima or subjacent media. In the experimental animal, the level of the potential is determined by the production of hyperlipemic hypercholesteremia. In general, no significant disease occurs in an otherwise normal system unless the level of blood cholesterol exceeds about 350 mg. per cent.[4, 6, 10, 13] In order to obtain a distribution approaching that common in man, much higher levels are required and must be maintained for many months. Even under these conditions, the pattern does not reduplicate that which is common in man, and, usually, a general lipid storage disease develops.

It is well-known that intimal lipoidosis usually begins in early life in man and that the blood cholesterol levels may be no greater than 150 to 200 mg. per cent in young adult or old patients with conspicuous atherosclerosis. Furthermore, in man, the arterial systems ordinarily seriously involved are those which also undergo a simultaneous medial calcific degeneration with intimal mesenchymal activation. When a similar situation is produced in experimental animals under appropriate conditions, medial calcific degeneration leads to fibrocellular intimal proliferation and thereby increases the lipoidosis potential, resulting in lipid localization at blood cholesterol levels regarded as normal for man. In order for this to occur in an impressive way in a few days or weeks, it is necessary that intimal mesenchymal proliferation be active. If the proliferation is allowed to mature and form a fibrous plaque before the serum cholesterol levels are increased to 180 to 250 mg. per cent, the lipid localization is negligible and often the lipoidosis potential is decreased to a level less than that of the adjacent normal arterial wall. This decrease of the lipoidosis potential over large areas of the aorta is, strangely enough, an apparent factor in increasing the probability of lipid accumulation in the more peripheral arterial systems. It seems that, if the most elective sites for lipid accumulation are rendered resistant, the next most elective sites are affected. This may be an explanation for the normal spreading pattern of intimal lipoidosis in the purely hypercholesteremic animal.

A similar curious effect is noted in studies of the distribution of calcific medial degeneration. The pattern is clearly defined in hypervitaminosis D. It varies among animals in which there are different combinations of hypervitaminosis D and hyperlipemic hypercholesteremia. Animals with moderate hyperlipemic hypercholesteremia are more resistant to the effects of viosterol. If the intimal lipoidosis is well developed before institution of the viosterol regime, the media of arteries beneath thick lipid plaques is protected from calcium deposition. In general, cellular lipoidosis either inhibits calcium deposition or accelerates its resorption. However, in these instances, calcium deposition is enhanced in the walls of peripheral arteries not affected by lipoidosis. Thus, again, it seems that, when elective sites for calcium accumulation are otherwise occupied or protected, there is a tendency for calcium to accumulate excessively in less elective sites. This may explain the spread of medial calcific degeneration in hypervitaminosis D. Inferences may also be drawn in connection with the vagaries in distribution of medial calcific degeneration and fibrous or fibroatheromatous intimal disease in man.

A common feature of intimal lipoidosis and subjacent medial lipoidosis in uncomplicated hyperlipemic hypercholesteremia in animals is the inconspicuous nature of mesenchymal reactions even in the presence of advanced cellular degeneration. It would seem that fibroblasts and endothelial cells are converted into foam cells laden with lipids and, as such, have little tendency to form collagen, elastic tissue, or a rich capillary plexus. A similar influence on mesenchymal reactions excited by medial calcific degeneration in hypervitaminosis D is noted in the presence of hyperlipemic hypercholesteremia. In all repair processes, whether in the media or intima, lipid localization becomes apparent and is accompanied by an inhibition of fibrogenesis and capillarization.[12, 16] However, the activation of proliferating mesenchymal cells by the lipids in some way inhibits progressive calcium deposition or accelerates its resorption. This is apparent also in many locations outside the walls of arteries.

Summary

If the pathogenesis of human atheroarteriosclerosis is governed by factors which produce the disease in experimental animals, the following rules should apply:

1. If a normal arterial system in man is subjected only to prolonged hyperlipemic hypercholesteremia, the consequences should be as follows:

   a. If the blood cholesterol values do not exceed about 350 mg. per cent, no significant disease should occur.

   b. If the blood cholesterol values approach about 500 mg. per cent, significant intimal and medial atherosclerosis should occur. The distribution of the disease should be fairly uniform, and the pattern should resemble that described in several animal species.

   c. If the blood cholesterol levels significantly exceed 500 mg. per cent, the severity of the atherosclerosis should be correspondingly increased and complicated by increasing evidence of a general lipid storage disturbance before significant atherosclerosis becomes apparent in many arterial systems routinely affected in man with normal cholesterol levels.

   d. The accumulation of lipids under the preceding conditions should be, as a first approximation,

directly proportional to the duration and magnitude of elevated blood cholesterol values.

e. As lipids accumulate, degenerative changes should occur, and these in turn should excite abortive reparative changes. The principal end result in the intima should be a relatively acellular mass of amorphous and crystalline material composed principally of lipids enmeshed in a hyalinized avascular fibrillar network. A similar result in lesser degree should occur in the media of some arteries, occasionally with minimal vascularization. Calcium accumulation should be evident in the deteriorated intimal lesions but negligible or absent in the media.

2. If a degenerative arterial system undergoing regeneration in man is subjected to prolonged hyperlipemic hypercholesteremia, the consequences should be as follows:

a. If the blood cholesterol values do not exceed about 150 mg. per cent, no significant atherosclerosis should occur.

b. If the blood cholesterol values approach 200 to 250 mg. per cent, significant atheromatous accumulations should occur. The distribution of the accumulations should be determined by 2 principal factors: (1) the nature of the arterial degeneration and reparative reaction and (2) the normal lipoidosis potential of the arterial segment undergoing degeneration and repair. In general, the more active the mesenchymal reparative reactions in the intima and, to a lesser extent, in the media, the greater the probability of significant lipid accumulation. In the same sense, the more complete the reparative reactions, the less the probability of significant lipid accumulation. Hence, unless all parts of the arterial system are at the same stage of degeneration and repair, the pattern of atheromatous deposition in arteriosclerotic lesions should be variable and different from that produced in a normal arterial system by hyperlipemic hypercholesteremia alone.

c. If the blood cholesterol values approach 250 to 350 mg. per cent, excessive atheromatous accumulations should tend to occur in a manner governed principally by the 2 factors mentioned above.

d. The accumulation of lipids under the preceding conditions should not necessarily require months or years. Under optimal conditions, significant intimal lipoidosis in activated mesenchyme should occur in a few days. The lipoidosis occurring in this brief time may be far in excess of that expected in a much longer time at much higher cholesterol levels in the absence of activated mesenchyme. On the other hand, under the least optimal conditions, significant intimal lipoidosis in activated, mature intimal mesenchyme may proceed more slowly and to a lesser degree than lipid accumulation in adjacent normal intima.

e. If the degenerative changes in the media are accompanied by calcium deposition and if the blood cholesterol values remain below 150 mg. per cent, certain arteriosclerotic sequences should be expected. Excitation of reparative mesenchymal reactions in the media, largely through penetration of vascularized adventitial mesenchyme, should result in active resorption or ossification of the calcified medial structure. At the same time, avascular intimal proliferative reactions should result in a fibrocellular structure resembling, in some respects, an arterial wall.

f. If the sequences indicated above proceed in the presence of blood cholesterol values at which significant lipoidosis complicates the reparative reactions, certain trends should occur: (1) the accumulation of lipids in the newly formed medial mesenchyme should retard vascularization, inhibit fibrogenesis, and accelerate resorption of calcified medial structure and (2) the accumulation of lipids in the newly formed intimal mesenchyme should inhibit fibrogenesis, enhance the hyalinization of fibrillar structure, and interfere with the formation of a new vascular wall within the degenerate calcific shell of the artery. These effects should be particularly pronounced wherever the amorphous and crystalline lipids have accumulated in significant amounts. It is only in such locations that the tendency to calcification becomes evident. Viable lipid-laden mesenchymal cells resist calcification and even enhance the resorptive mechanisms.

g. As these various factors display antagonistic and synergistic influences, the broad spectrum of variable distribution and character of atheroarteriosclerosis can be predicted with fair accuracy in animal or man. Among the less well-recognized or established factors leading to inaccurate prediction is the tendency for lipids or calcium to accumulate in the most elective site. If the elective site is replete or otherwise resistant to accumulation, the lipids or calcium then tends to accumulate in the next most elective site. If this is true and not an error in our experimental observations, the spread of atheroarteriosclerotic disease in all of its central and peripheral variations may perhaps be more clearly understood.

h. Despite exaggerated and severe combinations of atheromatous and calcific arteriosclerotic diseases studied experimentally, nonembolic mural fibrinous occlusive thrombosis was unimpressive. The frequency of this complication in human atheroarteriosclerosis must therefore require conditions not satisfied by experiment. Among these conditions, the two which seem to be most important are the frequency of ulceration and of vascularization of intimal atheroarteriosclerotic lesions in man.

i. These considerations do not exclude the probability that variations from prediction should occur and that unknown local or systemic factors must then be sought to explain them.

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HEMODIALYSIS should not be withheld because of advanced age alone. Considerable benefit may be expected in patients over 60 years of age with chronic or acute renal failure unless an incurable or fatal condition, such as ruptured aortic aneurysm, major cerebrovascular accident, or carcinoma, is also present. Control of fluid and electrolyte balance, close medical observation, and administration of drugs are essential.

Of 12 patients with potentially curable acute uremia, 9 survived after hemodialysis; 1 died of pneumonia, 1 of heart disease, and 1 of massive gastrointestinal bleeding. Of 6 patients with potentially curable chronic uremia, 4 survived; 1 died of pulmonary edema with paralytic ileus, and 1 as a result of inadequately treated chronic pyelonephritis.

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CHARLES V. LAIR, PH.D.
Chief, Clinical Psychology Service
Veterans Administration Hospital,
Knoxville, Iowa

J. D. SMITH, M.ED.
Chief recreational therapist
Veterans Administration Hospital
Fayetteville, Arkansas

ANDY N. DEATON, M.D.
Staff physician

Combined group recreation and psychotherapy for hospitalized geriatric patients

Geriatric patients are often hospitalized longer than necessary because social and emotional maladjustment is not treated as part of the medical problem. A general hospital can use a therapeutic program to supplement the medical care of elderly patients.

A review of the literature on aging[1-5] underscores the necessity for research on treatment and rehabilitation. The typical geriatric patient presents a complex of physical, psychologic, and social maladjustments that challenges the ingenuity of both practicing therapists and experimentalists. A number of authors have made empiric observations and drawn tentative conclusions about the older hospitalized patients and their impairments and strengths and have offered possible solutions to the rehabilitation question.

It is generally recognized that the patients are regressed and poorly motivated. Such symptoms as dependency, irritability, hypochondriasis, depression, and suspiciousness become paramount. Furthermore, such patients become isolated in contrast to their healthier peers, who maintain a higher degree of social awareness, activity, and interest in work or hobbies.[2]

In order to counteract maladaptive responses to stress, it has been suggested that a combination of psychotherapy and recreational therapy, with an emphasis on group technics, can lead to at least partial restitution of damaged personalities and result in greater self-sufficiency among many of these elderly patients.[1,3,4]

This paper concerns an experimental group therapy program for middle-aged and geriatric patients. The rationale of the therapeutic endeavor is based on the idea that satisfactory adjustment in the older patient hinges on socialization, activity, interests, and maintenance of motivation and goal direction. It is hypothesized that treatment specific to these aims would aid in rehabilitating older chronic patients and result in less

need for frequent or prolonged hospitalization.

Procedure

Selection of patients. The selection of suitable patients for this experiment was a joint responsibility of the staff physician and the clinical psychologist. Criteria for selection were age and capacity for cooperation. Patients had to be between the ages of 50 and 70 years, though exceptions were made in two instances to fit the needs of specific patients, these being 47 and 78 years of age, respectively. Capacity referred to both psychologic and physical capability to cooperate and to be able to participate without undue risk. Persons with infectious diseases were not accepted, with one exception: a case of active tuberculosis was found after the study was started.

Aside from these 3 restrictions, patients were chosen at random from a general medical ward in the Veterans Administration Hospital. There were 50 patients in the program from February to June 1959. Five patients were dropped from statistical treatment—1 because he has remained on the hospital roll in order to receive treatment for leukemia and the other 4 because they were in the group for less than one day, either because of refusal to participate or because of discharge from the hospital.

The amount of time spent in therapy ranged from less than one week to six weeks, the median being 8.3 treatment days. The 45 patients were divided at the median line into 2 groups for purposes of statistical treatment. The average age of those in group I, who were treated less than 8.3 days, was 60.9 years and of those in group II, who were treated more than 8.3 days, 65.1 years.

Description of therapy program. The 3 major areas of therapy were medical care, psychotherapy, and recreational therapy, the latter involving both hobby crafts and light physical activities. An open-ended group approach was used in both psychotherapy and recreational therapy, thus allowing patients to be admitted or discharged, as deemed appropriate. Every effort was made to individualize the process without sacrificing the welfare of the total group. For example, a patient with a cardiovascular disease was not expected to compete in physical activity with a neurodermatitis patient. In short, the therapeutic goals were organized around individual capabilities in a group setting. The contribution of each treatment modality was as follows.

Medical care. The medical treatment of each experimental subject was individualized under the direction of a staff physician and, in some cases, incorporated such ancillary services as physical and corrective therapies. A wide variety of diagnoses was represented in our subjects. To make this discussion more meaningful, they were classified according to related disease groups.

Arteriosclerotic disorders were routinely diagnosed on the basis of an electrocardiogram and a serum glutamic oxalacetic transaminase test, after which a variety of therapy was used, depending on the nature of the condition and the degree of heart failure. Respiratory disorders were diagnosed by roentgenographs and physical examinations. Treatment hinged upon the severity of the illness. When the diagnosis was established, bronchial dilators and antiasthmatics were used. Patients with gastrointestinal disorders were studied by roentgenogram, using gastrointestinal and gallbladder series. Necessary treatment was given as indicated. Special diet was an important aspect of treatment in most cases, but antispasmodics were prescribed in certain cases. The mus-

culoskeletal disorders were primarily arthritic. Physical and drug therapies were used. Diabetes was the only endocrine disorder among these patients, who were placed on special diets, depending on their size and state of nutrition. In more severe cases, insulin controlled blood sugar levels, and some patients with milder cases received Orinase. The few neuropsychiatric patients in the group were in anxiety-depressive states and were given sedatives.

Group psychotherapy. A clinical psychologist directed group psychotherapy in 2 one-hour sessions weekly. Therapeutic efforts were concrete and circumscribed by the immediate experiences and worries of the patient, since the objective was not to produce a profound personality change but to alleviate feelings of insecurity with an attempt to capitalize on already present physical and psychologic assets. Fundamentally, this was a directive approach; however, patients were encouraged to discuss and help one another resolve conflicts involving rejection by their children, concern over financial problems, the useless feeling that often follows retirement, or whatever personal complaints they might verbalize. The following case is illustrative of the procedure employed.

A 63-year-old white widower came to the hospital within three weeks after a son, who for some years had been psychotic, committed suicide. Complicating his depressive reaction was the fact that he was diabetic and, due to his psychologic condition, refused to keep to his diet, usually rejecting his food. In group psychotherapy, he was first given an explanation of the meaning of depression, its symptoms, and what outcome could be expected. The patient was mute and withdrawn at first, and only after he had been in the group for several sessions was he encouraged to join in the discussion by being asked such simple questions as, "What do you think about D's situation?" After the patient began to show some response to these impersonal questions and started to initiate comments of his own, he was encouraged to reveal some of the personal problems that led up to his hospitalization. Gradually, he divulged the fact that he and his son had had an argument preceding the boy's suicide; the patient felt guilt over the possibility that he was at fault for his son's death. He had made great plans to establish a business in partnership with the son to secure his own future as well as to aid the son.

The outcome, then, was not only the death of the son but also a shattering of his own plans for security in old age. After this was expressed in psychotherapy, other group members lent considerable support in reassuring him and in trying to distract his attention from himself to the daily activities of the group. Encouraged to take up a hobby in recreational therapy, he found both ceramics and leather tooling to his liking. In physical activities, he chose archery and shuffleboard as his main interests. These pursuits are types of activities that allowed him to expiate guilt feelings and turn hostility outward, so that he felt less need for self-punishment. Should he not have selected such activities as these, they would have been specifically assigned to him and the reasons would have been discussed in the group. As his cooperativeness in psychotherapy and recreational therapy increased, he began to adhere more closely to his diabetic diet, and his mood was obviously better. After five weeks in the group, he was discharged from the hospital with his diabetes under control and with only mild residuals of his reactive depression.

In every instance, the aim of group psychotherapy was to help the patients face reality. They were encouraged to talk with one another and to form friendships within the group. Constructive goals, such as using the knowledge of leatherwork, ceramics, or whatever they liked to establish as a hobby, were suggested. The possibility of earning extra money by selling the products was pointed out. The patients were informed about their physical and mental conditions so that they could set limits on their activities and thus give up unrealistic striving toward objectives which frequently exceeded what they could have done as 20-year-olds and which, in fact, represented compensatory fantasy. On the other hand, they were encouraged to work up to their limits and not to stop because of their fears of failure or rejection.

Recreational therapy. A recreational therapist supervised this aspect of the program, though ample use was made of volunteers who were essential to the success of the program because of the limited staff personnel. The patients attended recreational therapy for an hour both in the morning and in the afternoon four days each week.

Morning sessions were devoted to hobbies and crafts. The aim was not to prescribe specific activities for special physical or psychologic conditions but to motivate and foster the development of interests in hobbies and games. On occasion, patients with particular problems were given suggestions and assignments. For instance, patients with arthritis who had finger joint involvement were encouraged to work with clay, weave, or do other appropriate exercises to keep their fingers active. Depressed patients were asked to do such things as leather tooling to help externalize aggression and frustration. If a patient was too dependent, he was forced to make simple decisions for himself and to work on his own individual project. An excessively independent patient was requested to help a more physically incapacitated one in order to strengthen cooperative attitudes. Actually, as each patient presented a unique set of problems, a common-sense approach had to be used to meet each individual situation. Most of the materials for the crafts and hobbies were donated by veterans' organizations, fraternal groups, and individuals.

The afternoon sessions consisted of physical games that patients could do for the sake of exercise as well as for diversion. For the first time in their lives, many of our subjects, who were drawn from low-income areas, found themselves absorbed in such activities as archery, croquet, darts, and shuffleboard. Special care was taken to see that none of the patients overtaxed himself; it was found that even several wheelchair patients developed the desire to get up and do things for themselves. Also, it was found that most of those who were too sick or paralyzed to leave a wheelchair could shoot a bow and arrow or do almost anything that their confreres who were able to stand could do. One patient, for instance, who had especially liked to fish before his stroke, learned that he could use a bait-casting rod from his wheelchair. With this knowledge, his mood rapidly improved and he requested a discharge so that he could go home and fish. It was our experience that often surprisingly little was needed to remotivate our patients.

Results

In order to evaluate the outcome of this program, the criterion of readmission to the hospital was selected. Since the study was done in a Veterans Administration Hospital that serves a specific geographic area, it seemed safe to assume that any patient who had need of further hospitalization would be most likely to return there. Furthermore, with the total number being divided at the median for statistical treatment, it was assumed that chance would make it as likely for members of one group to go to another hospital as for the other, thus balancing any differences. The median amount of time in the group happened to be about two weeks, which gave us a limited therapy group of 25 (group I) and an extended therapy group of 20 (group II). A check of the hospital records was done to determine which patients were readmitted within nine months after their discharge, and this was used to establish a standard of measurement. The results of the analysis of this data are shown in the table.

A biserial correlation was computed to determine the degree of relationship between time spent in the group and frequency of rehospitalization. The r_{bis} =0.42, and PE_{rb}=0.047.

Discussion

It is felt that the relationship between time spent in group therapy and necessity for rehospitalization can be accepted as having a sufficiently high positive correlation to support at least tentatively the original hypothesis of this paper, that is, that treatment aimed at socialization, motivation, and therapeutic counseling in a group setting can reduce the need for frequent and prolonged institutionalization in selected cases. However, the question of whether the diagnosis of one group favored rehospitalization more than that of the other group might be raised. A list of the diagnoses was submitted to a qualified physician not otherwise involved in this study. It was his judgment that the members of one group were no more likely to need rehospitalization within nine months of original discharge than the other. It is believed, therefore, that no material difference in severity of illness between the two groups could account for the observed differences in rehospitalization.

It is recognized that the correlation is low and accounts for only a small amount of the variation between the groups. However, this is to be expected, because (1) most of these patients have been chronically ill for a number of years and (2) perhaps, even under the most favorable circumstances, the program is incomplete. It is felt that an addition of posthospital counseling could lead to some form of vocational aid to provide facilities to continue that which had been started in the hospital. This could prevent further regression after the patient returns home. Another point which might be brought out is criteria for selection of patients. At this time, it is difficult to ascertain whether certain patients have more to gain than others because of either basic personality differences or the nature of the physical limitation. In any event, the results of this study have been encouraging enough to warrant more thorough experimental investigation into the interdisciplinary approach of treatment and rehabilitation for the geriatric patient.

Summary

This study is an investigation of 45 white male patients who were considered middle-aged or geriatric general medical problems and who were treated through an interdisciplinary rehabilitation program that included medical care, group psychotherapy, and recreational therapy. Nine months after the last of these patients had been discharged, a number of them had returned for rehospitalization. A correlation between the amount of time spent in the rehabilitation program and the

Length of time in group as compared to rehospitalization within nine months from discharge from therapy

	Rehospitalized	Not rehospitalized
Treated less than two weeks	13	12
Treated more than two weeks	5	15

necessity for rehospitalization was significant and positive. In other words, those patients who had been given a longer period of rehabilitation therapy tended to show a lower rate of return to the hospital. It is concluded that a rehabilitation program such as this is worth more thorough investigation and offers a potential in meeting the increasing demand for means to facilitate progress in medical treatment and better posthospital adjustment for elderly patients.

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IN SENILE DEMENTIA, atrophy of the cortical neurons before degeneration of other vital body tissues seems to be the essential pathologic lesion, with the cause unknown. Cerebral cardiovascular degeneration, while accentuating the condition, almost certainly is not the main cause, and constitutional, dietetic, toxic, and other factors may be more important contributors. Every case should be assessed carefully and some form of active treatment should be considered, since a condition resembling advanced dementia can be caused by a psychosis, a senile depression, an infection, a toxic condition, a slow-growing cerebral tumor, or a cerebral thrombosis or hemorrhage not involving the motor cortex. Avitaminosis or extreme anemia is sometimes found, and treatment can lead to substantial recovery. Once the illness is well developed, most patients do best in a hospital in the company of others similarly afflicted. The move to the hospital, however, should be made before the patient is too mentally disabled to adjust to change.

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Conducted by
MARTIN G. GOLDNER, M.D.
Edited by
BENJAMIN WAINFELD, M.D.

Acromegaly

A medical conference from the Jewish Chronic Disease Hospital Brooklyn, New York

▶ DR. GOLDNER: Acromegaly seldom presents any problem in differential diagnosis because of the classical appearance of the patient. Of considerable importance, however, are the questions of how and when to offer treatment. Equally important are the assessment of the complications of the disease and the problem of prognosis in the individual case. The history of our patient should give occasion to discuss these aspects.

DR. MADRID: This 51-year-old woman was admitted to the hospital on December 2, 1960, with weight loss, weakness, tiredness, polydipsia, and polyphagia. The patient was essentially healthy until 1935, when, during a pregnancy, she became aware that her head, face, body, hands, and feet started to increase in size. The pregnancy continued uneventfully, and she gave birth to a normal male infant weighing 10 lb. 14 oz. She was in Cuba at that time, having migrated there from Europe in 1929. In 1946, she came to the United States, and she has been under constant medical observation ever since. Her body changes continued slowly (see figures I to IV); her hat size increased from 20 to 23, her engagement ring had to be enlarged several times, her shoe size increased from 4 to 6½, her voice deepened, the skin thickened, hirsutism developed, and she became annoyed by a buzzing sensation in her head.

No treatment for these symptoms was instituted until 1952, when the patient was hospitalized for bilateral submandibular swelling. The swelling subsided spontaneously, and she was told that her abnormal appearance was due to a pituitary disorder. Surgery was advised but refused. She was given x-ray therapy to her head over a period of several months. Since that time, she has noted no further change in her appearance.

Three or four years ago, polydipsia, polyphagia, polyuria, and loss of weight developed. The patient was found to have diabetes mellitus and was placed on a diet and given oral hypoglycemic agents and, finally, insulin. The diabetes was rather difficult to control. In the past three years, her weight has grad-

FIG. I. Patient, age 17, before her illness

FIG. II. Patient, age 26, after onset of disease

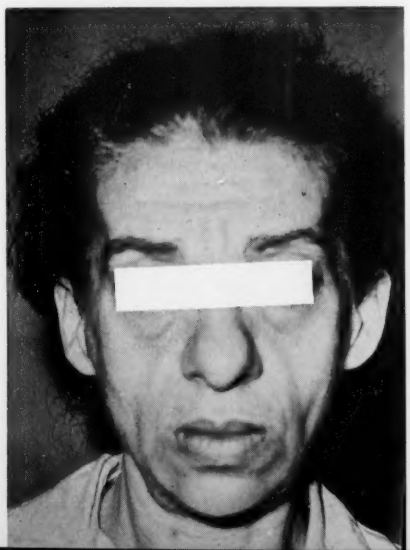

FIG. III. Patient, 1960

ually decreased from 141 to 123 lb. In recent years, she has noted intolerance of heat, and she prefers winter to summer. She also complains of palpitations and marked perspiration. She was thought to be hyperthyroid and has been treated intermittently with various agents, such as propylthiouracil, but she has not experienced any improvement in her clinical state. Her marked weakness and dyspnea on exertion necessitated the present hospitalization.

At age 11, the patient had pulmonary tuberculosis, which was treated by rest for two years. She has had psoriasis since age 12 and had gonorrhea in 1934. She was hospitalized in 1951 for a right oophorectomy and salpingectomy and in 1952 for bilateral submandibular swelling, as previously noted. In 1953, a mass was removed surgically from the left side of her neck, and in 1959, she was hospitalized for regulation of her diabetes mellitus.

The patient's menstrual periods began at age 14½, occurred every twenty-eight days, and were of five or six days' duration. In 1954, her menses became irregular, and her last menstrual period occurred three or four years later.

The patient has 1 child, still living, born full term, and had 1 induced abortion. Her father died of carcinoma of the rectum and her mother of arteriosclerotic heart disease. One uncle had diabetes mellitus.

On admission, the patient was found

FIG. IV. Patient's hands, 1960

to be well developed and well nourished but appeared chronically ill. Obviously, there was acromegaly. Blood pressure was 120/90; pulse, 88; and respiration, 20. Positive physical findings were multiple sebaceous cysts in the scalp; exophthalmos; large, protuberant tongue; well-healed surgical scar over the left sternoclavicular region; bilateral, firm, palpable submaxillary glands; diffusely enlarged thyroid gland, with the left lobe larger than the right; black pigmented area, about 0.5 in. in diameter, over the left anterior surface of the neck; left supraclavicular fullness, with no palpable nodes; harsh breath sounds heard at both lung bases; a well-healed appendectomy scar; psoriatic lesions on knees and elbows bilaterally; short, broad hands and feet; and bilateral varicosities of the lower extremities.

Laboratory examination revealed hemoglobin, 14.5 gm. per cent; white blood count, 3,600 per cubic millimeter, with normal differential; persistent proteinuria and glycosuria in the urine; and 20 to 25 white blood cells and 3 to 5 red blood cells per high-power field. Blood chemistry values were fasting blood sugar, 166; cholesterol, 372; cholesterol esters, 286, or 77 per cent; calcium, 11.4; alkaline phosphatase, 6.6; phosphatase, 3.4; total protein, 7.2; serum albumin and globulin, 3.8 and 3.4, respectively; thymol turbidity, 1; blood urea nitrogen, 14; radioactive iodine (I^{131}), 32.4 per cent in twenty-four hours; and basal metabolic rate, +1. Plasma 17-hydroxycorticoids were 14.9 mg. per cent, with rise to 47.4 mg. per cent after ACTH test; urinary 17-hydroxycorticoids, 9.8 mg. per twenty-four hours, with rise to 62.2 mg. per twenty-four hours after ACTH test; and urinary 17-ketosteroids, 22 mg. per twenty-four hours, with rise to 44 mg. per twenty-four hours after ACTH test.

Administration of SU-4885 (2-methyl-1,2-bis-(3-pyridyl)-1-propanone), an inhibitor of 11 B-hydroxylation of corticosteroids, was followed by a significant rise of the twenty-four-hour urinary 17-hydroxycorticoids and 17-ketosteroids to 38.4 and 47 mg., respectively. This indicates the ability of the patient's pituitary gland to respond normally to this agent by an increased production of ACTH.

DR. GOLDNER: I have asked Dr. Hessel to review for us the symptomatology of the disease and to analyze its course in our patient.

DR. HESSEL: This patient's history of acromegaly began during her pregnancy. This is not unusual. In the normal woman, there is physiologic growth of the pituitary during pregnancy. Upon delivery, there is involution of the pituitary to a size somewhat greater than that which preceded pregnancy. During pregnancy an acidophilic cell appears in the pituitary. This so-called "pregnancy cell" appears to arise from the chromophobe cells of the gland. There is also an increased incidence of onset and exacerbation of diabetes insipidus during pregnancy. Persistent lactation after pregnancy has been described, and, in fact, lactation without preceding pregnancy has been seen as well in this condition. Hypergenitalism as well as hypogenitalism may occur, and the latter may be accompanied by amenorrhea.

This patient began to have headaches in 1935. When confronted by this symptom in a patient with acromegaly, not only should mechanical pressure by tumor be considered, but bony overgrowth as well. The patient was markedly troubled by a sensation of numbness of the hands and increasing clumsiness in performing tasks which require a fair degree of dexterity. This symptom may be due to the overgrowth of soft tis-

sues of the hands, but, in a significant number of cases, is due to a carpal-tunnel syndrome. In the latter, there is overgrowth of the carpal ligament tissue with compression of the nerves of the intrinsic muscles of the hands. Resulting atrophy of the thenar and hypothenar eminences has been described. In this particular case, the symptoms were improved after x-ray therapy.

Other interesting symptoms which patients with acromegaly may have include polyarthralgia and arthritis, perhaps caused by marked bony overgrowth, enlargement of joint spaces, and serous effusions. More recently, the connection of peptic ulcer to acromegaly has been stressed, particularly in connection with multiple adenomas of the endocrine glands. Several patients with the Zollinger-Ellison syndrome (islet cell tumor with peptic ulcer), have been acromegalic.

The patient began to experience symptoms of polydipsia and polyuria. Here, the distinction must be made between diabetes mellitus and diabetes insipidus. The symptom of polyphagia is common in patients with uncomplicated acromegaly. It also may be accentuated in the course of diabetes mellitus and hypothalamic involvement.

Upon admission, the patient presented weakness and dyspnea on exertion. Of course, weakness in general is common in patients with acromegaly. It is interesting to note that, despite their rather robust appearance, acromegalic patients are weaker than the average population. Of course, other factors may be considered with such symptoms. These patients may be thyrotoxic or may have other endocrine abnormalities, such as hyperparathyroidism, hypoadrenalism, and diabetes mellitus. Heart disease is said to be common in acromegaly.[1] Until recently, the etiology of this heart involvement was not well understood. It was felt that the cardiac enlargement could be explained on the same basis as the visceromegaly which accompanies this disease. Recently, Hamwi and associates[2] and Balzer and McCullagh[3] reported a significant incidence of hypertension in acromegalic patients. The former[2] indicated that, in their series, hypertension and coronary arteriosclerosis accounted for a considerable amount of the cardiac involvement.

Our patient demonstrates some other common findings of acromegaly, including the large tongue, bilateral varicosities, and exophthalmos. The latter is seen commonly in acromegaly and is not necessarily accompanied by hyperthyroidism. The proteinuria and microscopic urinary findings may be on the basis of chronic pyelonephritis, which is common in diabetes. There is also an increased incidence of renal calculi in acromegalic patients.

Gershberg and associates[4] have described a case of acromegaly which demonstrated markedly enlarged kidneys with striking changes in both glomeruli and tubules at autopsy. Their patient's blood phosphorus was within normal limits. An elevated phosphorus has been assumed to be a good index of activity in acromegaly. However, it must be noted that, in the presence of uncontrolled diabetes or renal tubular lesions, there may be normal or low phosphorus levels in the presence of active acromegaly.

A few comments on the roentgenograms may be in order. There appears to be an increased incidence of hyperostosis frontalis interna in acromegaly. A recent series[5] showed this to be present in 27 of 28 cases. There may be marked increase in osteoporosis and reabsorption of bone. The size of the sella

turcica may not necessarily correlate with the clinical status of the patient.

Therapy includes radiation, surgery, and hormone administration and is reserved for patients who show one or more of the following criteria: (1) progressive acral enlargement; (2) progressive loss of visual fields; (3) persistent headache; (4) recent onset or exacerbation of diabetes mellitus; and (5) elevated serum phosphorus.

In most clinics, surgery is limited to those cases in which there is marked threat to loss of vision or signs of pituitary apoplexy and to those patients who have not responded to x-ray therapy. A few authorities prefer surgery as an initial mode of therapy. Hormonal therapy with estrogens would appear to be of use in milder cases or as an adjunct to surgery and irradiation.

DR. GOLDNER: Of special interest in our patient are the endocrine complications, diabetes and hyperthyroidism. Dr. Glick, what is the frequency of these complications in acromegaly and what is known or suggested about their mode of development?

DR. GLICK: This patient, as a result of her acromegaly, has disorders in 2 other endocrine systems. After acromegaly of twenty years' duration, the last few years of which were apparently inactive, the classical signs and symptoms of diabetes mellitus developed.

The association of diabetes mellitus and acromegaly has long been known. According to the most widely accepted statistics,[6] approximately 25 per cent of patients with acromegaly will have overt diabetes mellitus and another 25 per cent, abnormalities of the glucose tolerance curve or glycosuria. This is, however, not the universal experience; Luft[7] reports only 1 case of diabetes out of 50 of his patients with acromegaly, for example.

As would be expected, the acromegaly almost always precedes the diabetes. The interval between the onset of acromegaly and the onset of diabetes is variable. In a report of Coggeshall and Root,[8] this ranged between one and twenty years, with diabetes developing in the majority of patients within fifteen years. In our patient, the interval was about twenty years; this, though somewhat unusual, cannot be considered rare, as intervals of as long as thirty-seven years have been reported. In this case, however, the appearance of diabetes after apparent inactivity of the acromegaly is quite interesting.

Insufficient data exist in the literature to make a categoric statement about the significance of a family history of diabetes in these patients. The opinion has been expressed, however, that acromegalic patients with a family history of diabetes will have a higher incidence of diabetes than those without such a history. This variability in susceptibility is consistent with experimental data concerning the administration of human growth hormone to hypophysectomized patients.[9] A single small dose of growth hormone to a hypophysectomized juvenile diabetic patient will produce severe acidosis. Growth hormone administered for several days to a hypophysectomized, stable diabetic patient will produce marked exacerbation of the diabetes. Administration of growth hormone to a nondiabetic, hypophysectomized patient for a more prolonged period will result only in some decrease in glucose tolerance. Thus, those patients with the smallest insulin reserve will be most affected by the diabetogenic action of growth hormone.

Our patient had a maternal uncle with diabetes. In addition to this, her mother and some of her mother's siblings had arteriosclerotic heart disease;

in a woman, these data suggest a diabetic tendency.

There have been varying reports regarding the character of the diabetes observed in association with acromegaly. Some authors maintain that these diabetic patients do not differ from the usual maturity-onset diabetic, while others attribute certain special characteristics to the diabetes. Three of these characteristics have been stated in particular: (1) difficulty of control, (2) frequency of fluctuations of control, and (3) resistance to insulin. It must be borne in mind that these patients are ususally adults who probably have had an adequate supply of insulin up to the time of the onset of diabetes and thus might be expected to have the characteristics of stable diabetes. We believe that the difficulty of control in these patients is mainly caused by their enormous appetites, which make it most difficult to achieve any semblance of dietary control. The second characteristic mentioned, "fluctuation of severity of diabetes," is also probably largely a function of this polyphagia. But there is a more serious type of fluctuation which must be kept in mind. Sudden occurrence of hypoglycemia and marked insulin sensitivity may occur because of the development of hypopituitarism; this may have serious consequences if not immediately remedied.

With regard to the third characteristic of the diabetes, that of insulin resistance, no valid statistics exist. It is thought that the incidence of patients with severe insulin resistance, requiring several hundred units of insulin daily, is higher among acromegalics than among the general diabetic population. Our patient had been receiving 50 units of insulin daily with only fair control, but she can by no means be called brittle.

Statistics concerning the incidence of diabetic complications are few. Retinopathy has definitely been noted, but little has been reported on nephropathy. Our patient has albuminuria and signs of urinary tract inflammation of undetermined cause.

The pathologic physiology of the relationship between growth hormone and diabetes has not yet been fully elucidated. Until quite recently, no satisfactory human growth hormone was available for extensive research. Species differences, both in chemical and physical characteristics of the various growth hormones, are considerable. At the risk of oversimplification, the effect of growth hormone on carbohydrate metabolism may be divided into two opposing actions: an antiinsulin effect, either directly on the individual tissues or via an intermediate substance which acts at the tissue level, and stimulation of insulin secretion. In fact, some investigators attribute the diabetogenic effect of growth hormone to prolonged overstimulation and exhaustion of the beta cells of the pancreas. There are those who believe, though, that this latter insulin-stimulating effect is merely secondary, resulting from the normal body reaction to the hyperglycemia induced by growth hormone.[10] Acute administration of growth hormone can, under varying conditions, produce hyper- or hypoglycemia, dependent upon the predominance of either of the two effects. During the long-term administration of growth hormone, the diabetogenic effect predominates and is the one of clinical significance.

The thyroid, which is the other endocrine organ frequently affected in patients with acromegaly, is also involved in our patient. Although the thyroid-stimulating hormone is believed to be secreted by the basophil cell and the

overgrowth in acromegaly is due to secretion of the eosinophil cell, thyroid enlargement is quite common with acromegaly. This may merely be a reflection of general tissue growth in the body, but there may be a more specific action, the nature of which is unknown.

The most generally accepted figures report thyroid enlargement in 25 to 50 per cent of patients with acromegaly and an elevated basal metabolic rate in about 50 per cent.[11] However, true thyrotoxicosis is present in probably less than 5 per cent of the cases. Early in our knowledge of acromegaly, many patients with thyroid enlargement and acromegaly were operated upon for what was thought to be thyrotoxicosis. Pathologic examination of the excised thyroid revealed findings which were incompatible with thyrotoxicosis. While a small percentage of the thyroid glands examined may show toxic nodules, an overwhelming majority are of the colloid type, with focal, nontoxic adenomas and cysts.

The clinical diagnosis of thyrotoxicosis in the presence of acromegaly is extremely difficult. Increased perspiration and appetite and nervousness, for example, are common to both acromegalic and hyperthyroid patients. The basal metabolic rate, as previously indicated, is frequently elevated in the absence of thyrotoxicosis. Werner[12] postulates that difficulties in ventilation caused by anxiety and chest structure enlargement play a major role in this elevated basal metabolic rate. However, there may also be actual hypermetabolism. The serum cholesterol is of little aid. Insufficient data exist to evaluate properly the newer tests of thyroid function; the data available thus far indicate that they, too, would be of little value. McCullagh and associates[18] reported that the radioactive iodine (I^{131}) uptake was low or normal in their hypermetabolic acromegalic patients, even in the few thought to have true hyperthyroidism. Hamwi and associates[2] recently found that the protein-bound iodine (PBI) was actually lower in patients with active acromegaly than in those with inactive acromegaly. The one patient they had with true thyrotoxicosis and acromegaly had a PBI within normal limits. Their results with the I^{131} uptake were somewhat more encouraging but not enough to make the test a reliable aid in diagnosis.

Our patient may have had thyrotoxicosis one or two years ago, but since she was treated intermittently with propylthiouracil, this is difficult to ascertain. Presently, she is nervous, perspires excessively, and has palpitations and polyphagia. However, these symptoms are not recent and could be explained on the basis of acromegaly alone. She has gained 9 lb. during this past year and has constipation. Physical examination reveals only minimal exophthalmos, no tremor, slight tachycardia, and a nodular goiter. Her serum cholesterol is quite high, and both the I^{131} uptake and the basal metabolic rate are normal. It would have to be stated that her thyroid is not overactive at this time and that she probably has a nontoxic goiter.

A repeatedly quoted report regarding the surgical treatment of hyperthyroidism with acromegaly mentions a mortality of 18 per cent in 27 cases.[14] However, this was many years ago. One is led to believe, in reviewing that report, that some of the deaths might have been prevented had it been possible to utilize the therapeutic armamentarium of the present day. There have been no recent reports on sizable numbers of acromegalic patients undergoing thyroidectomy. The hazard that comes to mind when considering surgery in these

cases is the ever-present possibility of subclinical hypoadrenalism, with its potential for crisis under stress.

The most likely treatment for thyrotoxicosis, if present, would be medical, either with propylthiouracil or, preferably, with radioactive iodine. Data are insufficient to permit evaluation of the efficacy of therapy in these cases.

The adrenal glands frequently will have nonfunctioning adenomas at postmortem examination, but the finding of somewhat elevated steroid levels in this patient is interesting.

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PAIN SENSITIVITY apparently decreases with age. Comparisons were made of thresholds of pain perception and pain reaction for 90 subjects between 20 and 30 and 110 subjects over 65 years of age. The Hardy-Wolff-Goodell dolorimeter, a cutaneous heat-radiation apparatus, was used to provide the stimulus, with the forehead as the site of exposure. Stimulus was usually begun at 150 milligram calories (mcal.) per second per square centimeter and was increased gradually. Mean threshold at which subjects felt a beginning jab sensation was 251 to 263 mcal. for the younger and 319 to 323 mcal. for the older groups. The same age difference was found for values at which the first evidence of wincing was seen.

When findings for subjects were analyzed according to ethnic group, values for the Anglo-Saxons were considerably higher than those for the French and Jewish groups combined. Average reactions of the latter two groups were about the same. Differences between findings for men and women generally were not significant, although the average male subject had higher threshold values.

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MORSE P. MANSON, PH.D.
Chief, Counseling Psychology Services, Veterans Administration Hospital, Sepulveda, California

Study of a geriatric psychiatric population

Significant characteristics affecting hospital discharge

There are no significant differences relative to race, age, marital status, and number of diagnoses between geriatric psychiatric patients who remain in the hospital and those who are discharged. Motivation of staff members to move patients is a possible causative factor for discharge of patients.

A common medicopsychologic problem in the treatment of geriatric-psychiatric patients arises when such patients are prepared for discharge to families and communities. When the condition of maximum hospital benefits (MHB) is reached, many of these patients resist efforts effecting their movement from the hospital. Often, at this stage of treatment, patients mobilize massive resistance.

In rare instances, a patient states rationally and consciously that he feels more comfortable, secure, and happy in the hospital than he would at home. Therefore, he reasons, it is best to remain in the hospital. More often, patients do not consciously verbalize their motives for resisting discharge. Instead, they develop the "discharge syndrome," which consists of the recurrence of old or the presentation of new symptoms, increased demands for nursing and medical services, and a rapid return to former pathology. Sleeping nests of anxiety are aroused by awareness that discharge is imminent. In many other patients, as D Day approaches, exacerbations of quiescent mental and emotional states occur and irritability, belligerency, withdrawal, mutism, and threats of litigious actions follow. In some instances, a patient's belief that discharge will be painful and destructive of well-being and security results in malingering and deliberate obstructionism.

Nevertheless, geriatric psychiatric patients do leave hospitals and make satisfactory posthospital adjustments, as Manson and Engquist[1] have shown. Still, it cannot be denied that many such patients remain in the hospital for long

periods of time, even after attaining MHB.

This study describes characteristics of an aged psychiatric patient population as they relate to hospital discharge. The data presented answer the following questions:

1. What are some characteristics of a geriatric psychiatric patient population that remains in a Veterans Administration Hospital?
2. What are some characteristics of a geriatric psychiatric patient population that is discharged from a Veterans Administration Hospital?
3. Are there statistically significant differences between patients remaining and those who are discharged?
4. If significant differences do exist, what are they?

Method

All patients admitted to the Geriatric-Psychiatric Service, Veterans Administration Hospital, Sepulveda, California, from December 1955 to March 1959—an interval of thirty-nine months—were included in this study. The total population consisted of 275 male veterans. This group was divided into 2 subgroups: the remaining group of 195 patients and the discharged group of 80 patients. Ten characteristics of the 2 subgroups were compared. Findings are presented and discussed.

Subgroup comparisons

The 10 characteristics studied included: (1) race, (2) age, (3) marital status, (4) major occupation, (5) number of diagnoses, (6) kinds of diagnoses, (7) death rate, (8) time in hospital, (9) number of discharges, and (10) kinds of discharges.

Race. The 2 groups were predominantly white, and no significant differences in racial composition were found.

Age. The discharged group, on the average, was 3.1 years younger than the remaining group. However, this difference proved to be statistically insignificant, even though the trend indicated that a younger man has a better chance of being discharged than an older man.

Marital status. There were differences between the discharged and remaining groups relative to marital status. The discharged group had a larger percentage of single men and a smaller percentage of married men than had the remaining group. However, these differences were not statistically significant.

Main occupation. Using the *Dictionary of Occupational Titles* classification system, the main occupation of each patient, was coded and classified. Of the 275 patients, 231, or 84 per cent, had occupations which were coded and classified; 44, or 16 per cent, of the patients provided no information about their work, nor was this information available in their clinical records. Eighty-six different occupations were identified. The 3 principal occupations of the total group of patients were skilled work, 25 per cent; unskilled work, 9 per cent; and sales work, 8 per cent. The 3 main occupations of the remaining group were skilled work, 22 per cent; unskilled work, 10 per cent; and sales work, 9 per cent. The top 3 occupations of the discharged group were skilled work, 25 per cent; agricultural work, 11 per cent; and semiskilled work, 9 per cent. Table 1 presents the comparative figures dealing with main occupations.

When occupational group percentage differences were tested, only one significant difference was found: the remaining group had a significantly larger percentage at the .01 level of confidence in the category of building service. This indicates that men formerly employed as janitors or maintenance workers had

TABLE 1 **Main occupations**

Occupation	Remaining group		Discharged group		Total group	
	Number	Per cent	Number	Per cent	Number	Per cent
Professional	11	6	5	6	16	6
Subprofessional	4	2	4	5	8	3
Managerial	6	3	1	1	7	3
Clerical	14	7	3	4	17	6
Sales	17	9	4	5	21	8
Domestic	1	1	1	1	2	1
Personal service	5	3	1	1	6	2
Protective service	7	4	7	9	14	5
Building service*	9	5	0	0	9	3
Agricultural	11	6	9	11	20	7
Fishery	0	0	0	0	0	0
Forestry	0	0	1	1	1	0
Skilled	47	22	21	26	68	25
Semiskilled	10	5	7	9	17	6
Unskilled	19	10	6	8	25	9
Unknown	34	17	10	13	44	16
Total	195	100	80	100	275	100

*Percentage difference between remaining and discharged groups is significant at .01 level of confidence.

considerably more difficulty in leaving the hospital than did men who had worked at other jobs. The former work of a geriatric psychiatric patient has almost no influence in the development and activation of a discharge plan.

Number of diagnoses. The mean number of diagnoses for the remaining group was 2.4; for the discharged group, 2.2; and for the total group, 2.3. No significant difference between the remaining and discharged groups was found.

Kinds of diagnoses. The 3 largest categories of diagnoses for both the remaining and discharged groups were psychosis, chronic brain syndrome, and cardiovascular disease. Of the discharged group, 78 per cent had the diagnosis of psychosis; 50 per cent, chronic brain syndrome; and 26 per cent, cardiovascular disease. The remaining group had a larger percentage of both inactive tuberculosis diagnoses, statistically significant at the .01 level of confidence, and chronic brain syndrome diagnoses, statistically significant at the .05 level.

It is surprising to note no significant difference in regard to psychosis. Of the discharged group, 78 per cent carried this diagnosis. It thus appears that diagnoses of chronic brain syndrome and inactive tuberculosis markedly reduce the chances of obtaining a hospital discharge (table 2).

Death rate. A comparison of the death

TABLE 2 **Diagnostic categories**

Disease category	Remaining group		Total group		Discharged group	
	Number	Per cent	Number	Per cent	Number	Per cent
1. Psychosis	157	81	62	78	219	80
2. Incompetent	30	15	11	14	41	15
3. Senile deterioration	12	6	3	4	15	6
4. Psychoneurosis	12	6	7	9	19	7
5. Mental deficiency	2	1	1	1	3	1
6. Chronic brain syndrome*	113	58	40	50	153	56
7. Epilepsy	6	3	2	3	8	3
8. Parkinson's disease	3	2	2	3	5	2
9. Cardiovascular disease	40	21	21	26	61	22
10. Inactive tuberculosis†	25	23	4	5	29	11
11. Minor pulmonary disease	7	4	4	5	11	4
12. Gastrointestinal disease	5	3	2	3	7	3
13. Orthopedic disorders	17	9	5	6	22	8
14. Arthritic disease	6	3	1	1	7	3
15. Dermatologic disease	4	2	0	0	4	2
16. Sensory disorders	3	2	4	5	7	3
17. Cancer	6	3	0	0	6	2
18. Miscellaneous	16	8	5	6	21	8
Number patients	195		80		275	
Number diagnoses	464		174		638	
Mean number of diagnoses	2.4		2.2		2.3	

*Difference between discharged and remaining groups is significant at the .05 level.
†Difference between discharged and remaining groups is significant at the .01 level.

rates of the 195 remaining geriatric psychiatric patients and 56 discharged patients was made in a follow-up study. The death rate for the remaining group over a period of thirty-nine months was 18 per cent. For the 56 discharged patients over a period of forty-four months, it was 9 per cent, significant at the .1 level (table 3).

Total hospital stay. As might be expected, the discharged patients remained in the hospital for a shorter period of time. This group stayed for an average of 18.8 months, while the remaining patients averaged 25.2 months. The discharged group thus stayed, on the average, 6.4 months less than did the remaining group. This difference was significant at the .02 level. The mean time for the total group of patients was 23.3 months.

Number of discharges. Once again, as

TABLE 3 Percentage of deaths

Group	Number of patients	Number of deaths	Period of months	Per cent of deaths
Remaining	195	36	39	18
Discharged	56	5	44	9

might be expected, the discharged group had considerably more discharges than did the remaining group. The mean number of discharges for the former was 1.3 and for the latter, .1. The total group of patients had a mean of .5 discharges. On the average, the discharged group had 13 times the number of discharges as had the remaining group. This difference was significant at the .01 level.

Kinds of discharges. An analysis of the kinds of discharges was made. Of all discharges taken by the total group of patients, 79 per cent were taken by the group of 80 discharged patients, while 21 per cent were taken by the remaining 195 patients. Significant differences at the .05 level were found in the following types of discharges: the remaining group had a significantly larger percentage of trial visits, and the discharged group had a significantly larger percentage of MHB discharges and against-medical-advice discharges (table 4).

Characteristics of the 2 subgroups of geriatric psychiatric patients are compared in table 5.

Discussion

No real differences were found in the characteristics of race, age, marital sta-

TABLE 4 Kinds of discharges

Discharges	Remaining group		Discharged group		Total group	
	Number	Per cent	Number	Per cent	Number	Per cent
Trial visits*	14	50	35	34	49	36
Maximum hospital benefits*	5	18	32	31	37	28
Domiciliary	4	14	15	14	19	15
Family care	3	11	11	11	14	11
Against medical advice*	0	0	5	5	5	4
Elopement	2	7	3	3	5	4
Member employee program	0	0	2	2	2	2
Total	28	100	103	100	131	100

NOTE: Many trial-visit discharges later were converted to maximum-hospital-benefits discharges. Several patients on trial visit later went to family care. Some domiciliary patients also later went on family care.

*Statistically significant differences at the .05 level of confidence between remaining and discharged groups.

tus, or number of diagnoses. A single occupational category was significant. Of a total of 18 diagnoses, 2 were significant.

Significant differences were noted in the analyses of months in the hospital and numbers of discharges. Such findings could be expected if the remaining group was significantly more pathologic, but there was only slight evidence of this. It is only an assumption that the remaining patients are sicker than the discharged patients. This raises the provocative question, "If it is not illness that keeps a geriatric psychiatric patient in the hospital, what is it?" Another question would be, "What factors lead to hospital discharge of the geriatric psychiatric patient?"

An extremely interesting finding was the lower death rate for discharged patients. This indicates that an older psychiatric patient's fear of discharge, insofar as death is concerned, is unrealistic.

Although some differences between the remaining and discharged groups were found, no single characteristic or combination of characteristics could be recognized which made it possible to predict which patients would remain in or would leave the hospital.

Speculating on the factors which facilitated the movement of the 80 discharged patients, one condition, not described or studied but felt to have played an important part in the discharges, was brought out when the results of this study were presented to the staff. This was the belief, expressed by several staff members, that almost any

TABLE 5 **Comparison of group characteristics**

	Remaining group	Discharged group
Race	white, 95%; other, 5%	white, 94%; other, 6%
Age	28-88 years; mean, 62.4 years	25-82 years; mean, 59.3 years
Marital status	married, 46%; single, 29%; divorced, 18%	married, 39%; single, 33%; divorced, 21%
Main occupations	skilled workers, 22% unskilled workers, 10% sales workers, 9%	skilled workers, 26% agricultural workers, 11% semiskilled workers, 9%
Mean number of diagnoses	2.4	2.2
Major diagnoses	psychosis, 81% chronic brain syndrome, 58% inactive tuberculosis, 21% cardiovascular disease, 21% incompetent, 15%	psychosis, 78% chronic brain syndrome, 50% cardiovascular disease, 26% incompetent, 14% psychoneurosis, 9%
Death rate	18% over 39 months	9% over 44 months
Mean length of hospital stay	25.2 months	18.8 months
Mean number of discharges	.1	1.3
Major kinds of discharges	trial visit, 50%; maximum hospital benefits, 18%; domiciliary, 14%	trial visit, 34%; maximum hospital benefits, 31%; domiciliary, 14%

geriatric psychiatric patient who has been stabilized in his medical-psychiatric treatment can be helped to develop a realistic discharge plan if some significant member of the staff becomes strongly interested in him. When this occurs, a more comprehensive and integrated use of hospital and community resources takes place, and more staff time and discussion result. Such interest in a patient by a staff member stimulates other staff members, and soon a more meaningful and concerted team effort is exerted. In nearly all instances, patients respond by increased participation in the development of their discharge plans.

Thus, it well may be that the motivation of staff members to move patients is the most significant factor in their discharge from geriatric-psychiatric settings.

Results

1. A comparative study was made of 195 geriatric psychiatric patients who remained in the hospital and of 80 geriatric psychiatric patients who were discharged.

2. No significant differences were found relative to race, age, marital status, and numbers of diagnoses.

3. One significant occupational and 2 significant diagnostic categories were noted.

4. It was found that the remaining group had a significantly longer period of hospitalization. The discharged group had a significantly greater number of discharges.

5. The death rate of the discharged group was one-half that of the remaining group.

6. One suggested causative factor for discharge of patients is the motivation of staff members to move patients.

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PLACEBOS apparently are as effective as some ataractics in improving the mental health of geriatric patients with senile disturbances. Patients over 60 years of age with combinations of depression, paranoid ideation, restless agitation, or confusion were divided into groups of 16 persons each, according to whether they received (1) chlorpromazine, (2) reserpine-pipradrol, (3) deodorized tincture of opium, (4) a placebo, or (5) no medication. Anxiety decreased in the chlorpromazine and placebo groups over a two-month period but increased in the group receiving no medication. Patients in the placebo group improved in mood and spontaneity. Deterioration of condition in patients receiving neither placebo nor drugs emphasizes the need for a semblance of medication and care in a geriatric ward.

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EVERETT J. SOOP, A.M., LL.D.
Director, University Extension Service, and lecturer, School of Education, University of Michigan

University of Michigan extension service program in gerontology

The Extension Service at the University of Michigan has joined forces with the Division of Gerontology of the Institute for Human Adjustment and other units of the university to provide courses, conferences, consultative services, and various publications for their state-wide clientele of lay and professional groups and individuals who are interested in the many problems of the increasing number of citizens in the older age grouping.

The bylaws of the board of regents of The University of Michigan state that the University Extension Service shall be maintained for the purpose of providing educational advantages for residents of the state who are not in a position to pursue programs of study in residence at the University and that, in the planning and development of the educational programs of the Extension Service, the director and executive committee shall proceed in such manner and with such purpose that the University will make an effective and significant contribution to the educational services of the state through programs of activity which are representative of its distinctive position as a university. With these statements as a background, the Extension Service has developed various activities, including one in gerontology.

The Extension Service has no faculty of its own. Its many programs are natural extensions of ongoing, experimental, or research projects of the schools, colleges, departments, or special institutes of the University. It serves as the administrative agency through which these educational advantages are channeled throughout the state. The close relationship between the Division of Gerontology of the Institute for Human Adjustment and the Extension Service is the result of our mutual interest in a common clientele and in the development of means whereby the increasing number of Michigan citizens in the older age grouping might better be served. Although the usual number of preliminary discussions had probably taken place, the first recorded activity of the Extension Service in the field of gerontology

took place in the university year of 1947 and 1948 and drew its support from the president of the University, the director of the Extension Service, and the director of the Institute for Human Adjustment. Since that time, the extension program has developed parallel to the growth of the total program of the Division of Gerontology as that division's program has become nationally and internationally known. In fact, the Extention Service takes special pride in the assistance it gave in making possible three of the early, major publications produced by the division.

Courses. Gerontology was a new field in 1947 and 1948. Educational pioneering was necessary, as very little experimentation had been conducted and there was practically no literature on the subject. The usual basic questions were raised and plans were built on the basis of the introspective answers. What were the needs and what methods should be used in satisfying them? Were the people for whom programs were to be built located in one homogeneous group or were they in many groups, all having different characteristics?

The first project was a sixteen-week course for older people inaugurated in February 1948. The course was to be called "Problems and Adjustments in Later Maturity and Old Age," and the 8 topics to be discussed were "designed (1) to provide specific information for immediate use in connection with current individual problems, (2) to give a philosophy of aging, and (3) to afford some understanding of the relationship of the satisfaction of the needs of older people to the total social organization." The 8 broad fields of information covered were: biological aging, psychological changes, maintenance of physical and mental health, living arrangements, creative activities, religion, social and economic security, and legal problems. In general, the instructors were well-known members of the University faculty and, in practically all cases, were approaching or actually in the period of later maturity. The course carried no academic credit, and complete freedom was given the instructors in their methods of presentation. Fifty-one enrollments were received. Later, the course was repeated in Ann Arbor and was also offered in other communities. Additional instructors participated, but the course outline was approximately the same. The title, however, was shortened to "Aging and Living."

Courses have continued to be one of the important technics, but their structure has undergone many changes as experience has been gained. The number of sessions may or may not be 16, the exact number being determined by the type and amount of subject matter to be covered. Perhaps 6, 8, 12, or some other number may be sufficient.

In similar fashion, different courses are now planned for different groups. Whereas the first course attracted a heterogenous group, it also highlighted the specific needs and specialized interests of groups as determined both by their ages and occupations. One group might be considered as composed of persons over 65 who have voluntarily or have been arbitrarily retired and who are seeking to solve some of the problems attendant upon the transition to retirement, and another might consist of men and women of middle age who are interested in preparing for retirement. It was clearly evident that many younger couples are looking for assistance in solving the problems related to their aging parents, and these often involve attitudes toward aging, the actualities of three generations living in cramped quarters, and similar topics.

Needs of the various professions have also become more visible. Training in working with this fast-growing segment of our population has become sufficiently necessary to warrant classes or special seminars for doctors, pastors, teachers, counselors, social workers, personnel and employment staffs, and both managerial and labor representatives. The Division of Gerontology was one of the first units in the country to offer preparation for retirement to union personnel. One of the most recent developments has been the opening of courses offered by the Division of Adult Education, a cooperative program with Wayne University, to any person aged 65 or over for the payment of a $2 fee. The normal tuition is $20. Although the program is a new venture, enrollment exceeds 100 persons who are largely electing courses in foreign languages and the humanities.

Within all of these groups, experimentation has been continuous. As courses and course materials have been developed, they have been used in training projects and then have been made available to others having similar needs and interests. During the more than a decade since the Michigan program began, a great many other institutions and organizations have entered the field, but there has been no diminution in the number and variety of requests to this University for assistance.

Conferences. Courses are only one of the ways in which instruction has been provided. Others are conferences, consultations, publications, tape recordings, and radio and television programs. The first of what has since developed into an annual conference on aging was held on the campus during the summer of 1948. It was called the Charles A. Fisher Memorial Institute on Aging in honor of Dr. Fisher, the director of the Extension Service, who had been instrumental in helping plan the program but whose death had occurred before the time of the conference.

As stated in the program, the purpose was to "call attention to the problems of old age and to provide information through lectures, papers, discussions, and demonstrations to persons working with older people and to older people themselves." Although jointly sponsored by the Extension Service and the Institute for Human Adjustment, the conference was a part of the summer session program of the University. Faculty members and national authorities known to them were program participants. This initial venture was so successful that plans were immediately announced to make it an annual event. Through the years its reputation has continued to grow until it is now known as the outstanding national conference on gerontology.

The topic of last summer's conference, the twelfth in the series, was "Designs for Retirement." Some of the previous topics were "Social Gerontology and its Applications;" "Free Time: Challenge for Later Maturity;" "Health for the Aging;" "Aging—Applying Today's Knowledge Today;" "Aging—Everybody's Business;" "Earning Opportunities for Mature Workers;" "Housing the Aging;" and "Rehabilitation of the Handicapped Worker Over Forty." In practically all cases, these conferences have resulted in book-length publications which have had wide acceptance. The first three publications, often referred to as the "Older Years Trilogy," were originally published for the Extension Service by the University Press and were titled, *Living Through the Older Years, Planning the Older Years,* and *Growing in the Older Years.* Conferences have also been conducted in

university extension centers in other Michigan cities, the most notable being the Detroit program for women of middle age, *"The Age of Opportunity."*

Consultations. The Division of Gerontology's staff has been scheduled considerable time by the Extension Service to assist communities throughout Michigan in the development of projects relating to the problems of their senior citizens. Of special note was the planning done with a group of citizens in Grand Rapids. The resulting community survey and forum were reported under the title, "Older People Tell Their Story," and contributed greatly to the education of Grand Rapids and the state relative to our aging population.

Publications. Reading lists have been prepared and distributed on request. Other publications include a Living in the Later Years Radio Series, a Plan for a Community Center Program of Services and Activities for Older People, a discussion outline and series as part of a cooperative project with the Fund for Adult Education of the Ford Foundation, and several leaflets and pamphlets. Also, a number of programs on gerontology have been prepared by the University as part of its television broadcasting service. These have been photographed, and the resulting Kinescopes are available on 16 mm. film for showing to local groups.

The Extension Service has also experimented occasionally with recreational projects for older people. An orchestra was conducted one year, and "Over and Under 60" club was organized another year, tours were arranged, and an afternoon movie program ran for several months. With the increasing awareness of the citizenry, other institutions and agencies have entered the field. Looking ahead, it appears that gradually the University can withdraw from those activities which can and should be operated under other auspicies and focus still more of its attention on research and training professional personnel under lay leadership.

ONSET OF cold weather and rise in relative humidity may precipitate attacks of acute myocardial infarction in patients with coronary heart disease, according to a study of 298 patients hospitalized with coronary thrombosis. Barometric pressure apparently has no effect upon incidence of the disease.

In the study group, 3 times as many men as women had myocardial infarction, and mortality was highest among the older persons. Over 90 per cent of deaths occurred within fifteen days of hospital admission, which suggests that major therapeutic efforts should be expended during this period. Patients with low systolic blood pressure on admission had the poorest immediate prognosis.

A. O. ADESOLA: The influence of meteorological changes on coronary thrombosis. Brit. Heart J. 22: 635-641, 1960.

BEATRICE H. HILL
Director, Consulting Service on Recreation for the Ill and Handicapped, National Recreation Association, New York City

Here's what recreation can do for geriatric patients

Rehabilitative medicine has added years to lives, but little has been done to add life to years. Recreation can give mental and emotional employment to elderly persons. The result? Patients are happier and pose fewer problems in medical and psychiatric management. This article, based on a study carried out in institutions for the aged, indicates the positive effects of recreation on elderly people.

▶ Can a recreation program bring the withdrawn geriatric patient out of his shell? Will this kind of therapy actually help the senile patient to become less cantankerous, better oriented, and more cooperative?

These questions, no doubt, were in the minds of the four nursing home administrators whom we asked to participate in our one-year coordinated recreation project in rural Sussex County, New Jersey.

The administrators agreed that they had nothing to lose in letting us sponsor the program and admitted that they had much to gain if their elderly patients responded to recreation. And, during the project, many, many of the participants developed better attitudes, positive personality changes, and the ability to accept their limitations. The results were so significant that the nursing homes have continued the program on the coordinated community basis with each institution contributing to the cost.

What witchery did we use to change the so-called problem patients' attitudes? We didn't need any charms or good omens—just the sound, common sense principles of a qualified recreation director, who, in turn, passed his beliefs on to his volunteers. Philip Walsh applied the philosophy of his specialty: "Exercise patience, if necessary, for months. The patient will eventually reward you with his cooperation." Here are some examples of how the Sussex County project's director handled the geriatric patients.

Many of the elderly nursing home guests, as we know, refuse to leave their rooms. And, as one purpose of recreation is to teach patients the pleasure of

group living, the workers ask the patients to come to the recreation room for parties, games, movies, and the like.

One such patient said, "No, absolutely no," to group recreation twice a week for nearly two months. It was quite obvious that her own curiosity would not lure her out of her room and make her a joiner. So, the director interviewed her several times to find out why she refused. What was her reason?

The patient had lived in a hotel for twenty years and always had to pay or tip for extra services. She could not "afford" recreation. The director explained that there was no charge for the sessions and that the activities were "on the house." Once this was made clear to her, she began to enthusiastically participate in group activities and has been continuing to do so.

Finding out why a patient refuses recreation is a big part of a director's job. For instance, one woman would not join in group activities when she saw a teenaged volunteer: "I don't want to be around that young one. She reminds me of my granddaughter who never bothers to come to see me." The director suggested that the patient try one or two sessions despite the teen-ager's presence. The happy result? The woman has an "adopted" granddaughter; the volunteer, an "adopted" grandmother.

One 76-year-old woman just about barricaded herself in her room when the group activities were in progress. Despite this, the recreation director always went into her room and chatted with her briefly during the three weekly sessions in the home.

However, the day finally came when the director could not spare the time to talk with the patient as he was preparing the recreation room for a party. The woman knew that the director was in the building for she heard his voice. When the party was in progress, the patient came out of her room "to see what all the racket was about and to find out if 'that nice man' was all right." The director's patience had been rewarded again. Since that time, the woman has been leaving her room every morning and spending the day talking to other patients, watching television, and, of course, participating in group activities.

Two fellow patients disagreeing over a game of dominoes brought one oldster down from his ivory tower after his constant refusals to take part in games. When the argument was at its height, he forgot his shyness and come out of his room "to straighten those two out."

The withdrawn patients aren't the only ones who benefit from a nursing home recreation project. Movies, parties, singing, and music have brought many a disoriented patient back to the present. For example, one 80-year-old man, who didn't know one day from the other before the recreation program started, can tell that "today must be Tuesday because the volunteers were here yesterday (Monday), and they will be back again tomorrow (Wednesday)."

Recreation not only orients patients and brings others out of their shells, but it also helps those who seem incapable of amusing themselves when they are alone. One such patient used to sit by the window and brood in her free time. She was always "too tired" to sew, paint, or weave. However, she was very interested in a pocketbook that another patient was making—so interested that she wanted to buy it. The woman refused but suggested that the patient ask the recreation worker how to weave the leather strips into a change purse. The wisdom of the trained recreation director had been rewarded once more. The formerly recalcitrant patient has become very adept at handwork.

The recreation workers teach the patients arts and crafts, but, in one instance, the tables were turned: the patient taught the volunteer. "No young thing is going to teach me—not after I spent fifty years teaching." The sprightly 80-year-old woman instructs the volunteers on various types of needlework—knitting, crocheting, tatting, and embroidering. And the workers are glad to learn these additional skills.

Not all nursing home patients need so much attention and special handling, but the happy, well-adjusted guests are even happier and better adjusted with a recreation program. For example, one old sea captain looks forward to recreation sessions because the director swaps sea stories with him.

Another patient eagerly waits for his favorite volunteer who always brings him homemade cookies. One man, after seeing a movie about California left the recreation room saying, "That's sure a wonderful state. Never did get around to going there though, so I'm glad I saw this movie."

Movies, always a great favorite, have a special meaning to one oldster, a former mechanic. He watched the worker set up the equipment and recently said, "One of these days I'm going to start doing that for you."

Every nursing home has the patient who doesn't lose his sense of humor no matter how ill he might be. Recreation can be a springboard for him, too. When the recreation director told one such bedridden man that a magician would be in the home to entertain, he quipped, "Good, send him along up here. Maybe he can pull a cure out of his bag of tricks and I'll be well again."

Call it magic, call it witchery, call recreation anything you wish. It can give the patients in your home some of the happiest moments they've experienced in many years.

A FLUORESCENT STAIN differentiates cutaneous amyloid deposits from colloid milium and senile elastosis. Specimens are stained in a 1 per cent aqueous solution of thioflavine T for three minutes. Sections are then differentiated in 1 per cent acetic acid for ten minutes, dehydrated, and mounted in Harleco Synthetic Resin-xylene solution. With an ultraviolet light source, deposits of amyloid fluoresce with a distinct, bright blue color.

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A. K. KURBAN: Fluorescent stain for amyloid: an easy histological differentiation between cutaneous amyloidosis, colloid milium and senile elastosis. Bull. Johns Hopkins Hosp. 107: 320-328, 1960.

Elon Howard Moore

Pioneer in the sociology of aging and retirement

JOEL V. BERREMAN, PH.D.
Professor, Department of Sociology, University of Oregon College of Liberal Arts

▶ Among the scholars from many disciplines who contributed to the rapidly growing literature of geriatrics in its early phases, Dr. Elon Howard Moore deserves an honored place.

He brought to this field the objective approach of a trained social scientist and a broad background in sociology which included nearly thirty years of teaching interspersed and combined with research and active participation in the academic community. He taught on the faculties of the University of Illinois, Oregon State College, and the University of Oregon, serving as head of the sociology department at Oregon for twelve years. He was president of the Pacific Sociological Society and a member of its advisory council. He was active in the Social Science Research Council, where he was a member of the Committee on Old Age Research. He was, for a time, cooperating editor of the quarterly journal, *Sociology and Social Research*.

I knew Dr. Moore for twenty years as colleague, department head, and friend. He was a humble man and devoted to his wife, Marjorie, and their four children. His administration of the sociology department was a model of democratic leadership. His fairness and good judgment, his respect for the views even of the least of us, and his rare sense of humor won the admiration and loyalty of his associates and made him a gracious host and stimulating conversationalist. There was also a great strength about him. He had a deep sense of justice and, when this was aroused, he showed exceptional courage. He met personal misfortune with equal courage. As a young man, he survived a severe attack of polio and, despite the prediction of his physician and his friends, he was able, by sheer determination, to regain his full strength and vigor. He entered military service in World War I less than two years after the onset of this illness.

As a scholar, Dr. Moore was first attracted to the fields of criminology and penology and he made notable contributions to the psychology of testimony. He devoted many years to the study of population problems, and his broad scholarly interests also led to publications in social theory, community organization and change, education, and the sociological aspects of war and reconstruction.

His interest in aging and retirement came in the last decade of his active career, stimulated in part by his study of the changing age distribution of the population and in part, perhaps, by his own approaching retirement.

Dr. Moore's approach to this many-sided area was sociological, or perhaps sociopsychological. His primary emphasis was on the personal adjustment of individuals in retirement and during the declining years. Grants from his university and the Social Science Research Council enabled him to investigate the actual experiences of nearly a thousand retirees through interviews, questionnaires, and extensive correspondence over a period of years. He traveled across the country; talked with personnel directors in industry, education, and government; visited institutions for the retired; and conferred with other scholars in the field. During a sabbatical year, he lived in various communities of retired persons in Florida, Arizona, and California, participating in their activities and recording their conversations and behavior. He wanted to get the "feel" of his subjects and to understand their genuine reactions to retirement and the aging experience.

He published separate articles on the retirement experiences of impressive numbers of professors, ministers, businessmen, and industrial workers. From these studies and from his direct observations, he drew the generalizations which were embodied in his final book, *"The Nature of Retirement."*[1]

In this, as in his previous work, he applied his sociological insights to the problem of how to increase the satisfactions of aging persons, for, to his way of thinking, the breadth of life was at least as important as its length. He believed that normally active persons need not, and would not, be content to drop their lifetime activities and live in idleness. In his own words, "My thesis has been that retirement may be a condition of fulfillment and not decay, that what is left of a man's days can retain meaning and value."[2]

He saw the problems of the aging in broad perspective. Some stemmed from the changing nature of our society. Industrialization and urbanization were making obsolete the roles of older persons on the family farm and in the rural community. He viewed the later years as a normal stage in the life cycle. He did not decry these changes, but sought to discover ways of adapting to them. He observed that, as in any other period of life, adjustment in retirement depends heavily on what preceded it. "The retirement years," he wrote, "call for a pattern of life somewhat distinct and different from that which is found in the more productive years. Yet the degree of satisfaction which the retiree experiences in this period is dependent upon the habits and attitudes developed during the working years. We come to retirement with lives which are either enriched or starved in those attitudes and behaviors which give meaning and depth to life."[1] Those who are able to live within an income, who have genuine interests that can be followed after retirement, and who have learned to relinquish gracefully and develop compensations for the things which must be

given up make the most satisfying adjustment to retirement.

Dr. Moore was convinced by his studies that the answer to many problems of this last phase of life was preparation, not simply for financial security but in terms of attitudes, the planning of meaningful activities, and the development of interests. Such preparation should begin at 40 or 50, well in advance of retirement itself.

His publications, particularly his final book on this subject, were written with a sense of mission. They are replete with discussions of practical problems and how they have been successfully dealt with by the hundreds of persons whose experiences he has studied. Topics such as when to retire, where to retire, breaking with the past, substitutes for the job, and social relationships in retirement illustrate the down-to-earth character of his material. He describes the experiences and solutions of his subjects, explores the consequences of various modes of adjustment, and leaves his readers aware of the alternatives and able to make informed decisions for themselves.

Dr. Moore not only studied and wrote about retirement but was instrumental in organizing a Golden Age Club and establishing a program of recreation and other activities for the aging in the city in which he lived. At one time, he attempted to interest the administration of several universities in a program of training senior staff members for retirement. He planned his own retirement with keen anticipation, regarding it as an opportunity to apply his knowledge and to learn more by experience. The first months were in the nature of fulfillment. But he was to have little time, for his well-planned experiment was cut short five months after its beginning by his death.

Early in his professional career, Dr. Moore defined what to him constituted a contribution to scholarship. It embodied 3 operations: (1) the birth and testing of an idea, (2) the organization of the idea in relation to other ideas, and (3) the presentation of the idea and its relationships.[3] By his own criteria, Dr. Moore's work in the field of the adjustment of the aged must be counted a genuine contribution. He contributed substantially to the early growth of interest and knowledge in the social aspects of an aging population. His central idea, that the last phase of life can be a meaningful and rewarding one, was demonstrated by his studies. He related the problems of the aging to broad social changes and to the normal course of the life cycle. He communicated his idea and its supporting evidence to his fellow workers. Finally, he embodied his ideas in a book that presents to prospective retirees, as well as to other scholars, the results of his labors. He brought to bear on their practical problems not only the results of research but also the wisdom and insight of a thoughtful, sincere, and warm-hearted humanist.

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1. A.M.A. Council on Drugs: New and Nonofficial Drugs 1960, Philadelphia, J. B. Lippincott Company, 1960, p. 363.
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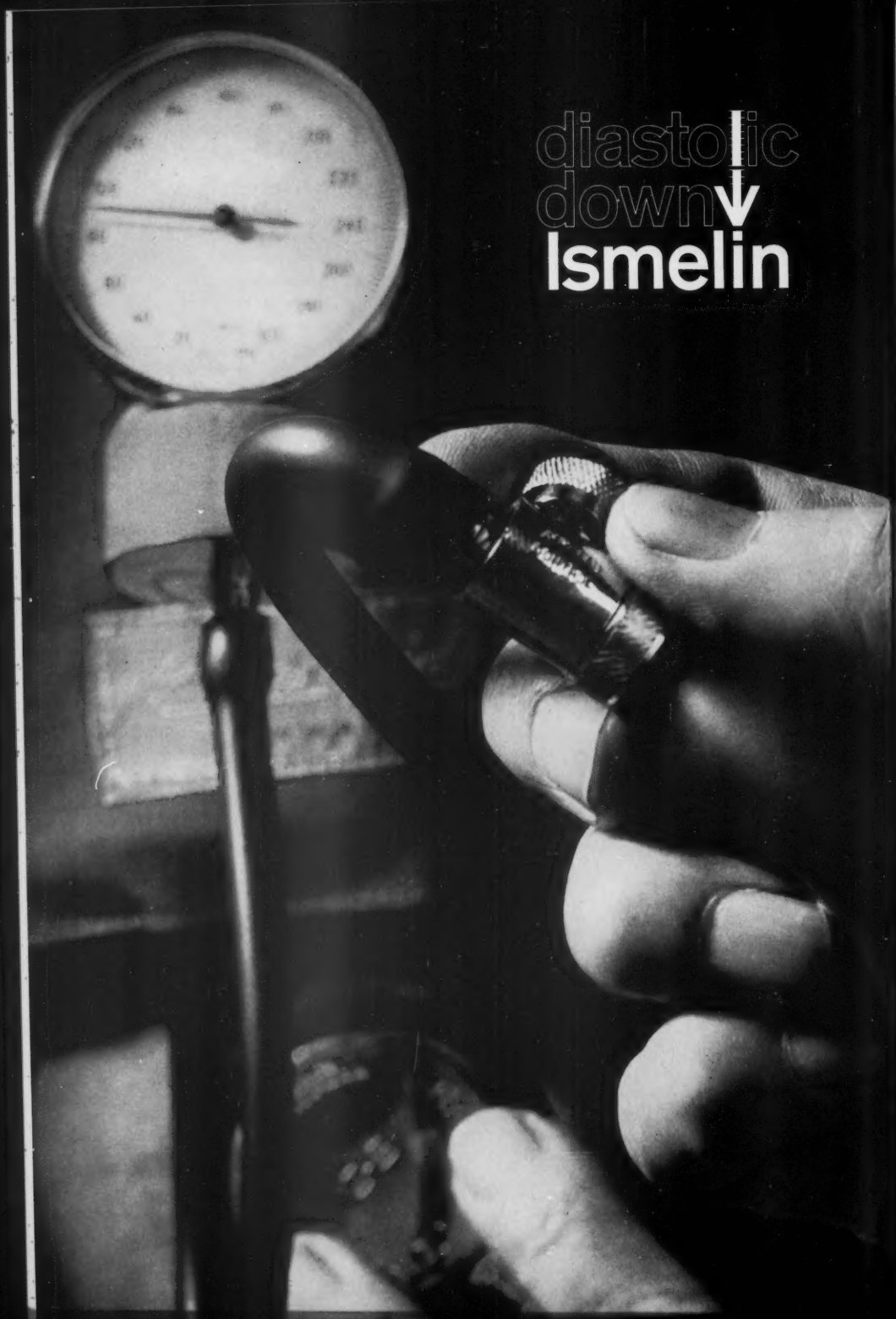
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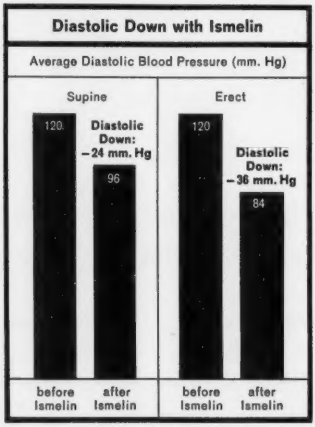

(Adapted from Riven and Hall[3])

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clinical briefs*

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Reference: 1. Bunim, J. J., in Hollander, J. L.: Arthritis and Allied Conditions, ed. 6, Philadelphia, Lea & Febiger, 1960, p. 364.

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Book reviews

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Aging: A Regional Appraisal

CARTER C. OSTERBIND, editor, 1961. Gainesville, Florida: University of Florida Press. 169 pages. $3.00.

The tenth annual Southern Conference on Gerontology, held at the University of Florida on March 16 and 17, 1961, is reported in this volume. The selected topics relate to various developments affecting elderly people and are concerned with their impact upon the South. Because of the sponsorship and location, more emphasis is placed upon Florida than on other areas of the region.

The book is divided into 4 sections: Part 1 identifies and describes social gerontology; part 2 relates the role of universities to regional needs; part 3 examines certain segments of social and economic life and special research affecting the aged in the South; and part 4 deals briefly with community action. While the focal point is one region, there is excellent general information on developments affecting every section of the United States.

As is often true in a volume of this type, there is variance as to the quality of the contributions and the amount of space devoted to each topic. The foci of the articles run the gamut from survey and research expressions, to theoretic summations of what could be done, to factual accounts of what is being done. The background of social gerontology, by Dr. Clark Tibbitts, and the roles of universities, as interpreted by Dr. Wilma Donahue, would be topnotch contributions to any volume and are worthwhile reading for all gerontologists. The impact of social security, by Dr. Ida C. Merriam, is classic, and other contributions, by Drs. Edgar S. Dunn, Jr., Irving L. Webber, Howard W. Carter, and Ruth E. Albrecht, demonstrate the increasing acceptance of research on the aged.

I was not so impressed, however, with the articles reproduced in part 4, with the exception of the paper by Margaret Jacks on suggestions for a statewide approach in serving the aged. Her comments were most exemplary. However, when I ran across anomolies by other authors, such as, ". . . I regret to say that our county still has a county-supported almshouse" and, in the next sentence, "We now consider it a modern nursing home," I became confused. This confusion was extended further by a discussion in an article on Salhaven, a retirement village sponsored by the Upholsterer's International Union of North America and probably, although not so stated, for retired members of the union. I was impressed with the general basic services purported to be offered but was curious as to how many residents are being served. And, if it is true that a basic principle of the board of managers is to ". . . allow the aging resident to remain independent and in his own home as long as possible . . . ," is this a principle the International espouses for those still residing in their own communities? And how many applicants have been rejected, for what reasons, and what then becomes of them? I raise these latter questions only because the village is interpreted as striving to meet the basic needs of its residents. Who, then, is not accepted, or is the village geared to meeting only some of the needs of only a few of the retired upholsterers?

(Continued on page 72A)

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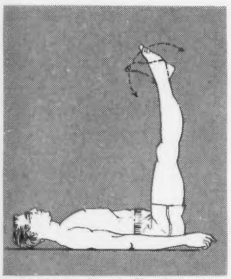
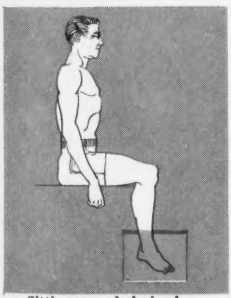
This easily performed clinical test[1] demonstrates the presence of peripheral arterial insufficiency, and to some extent the degree of circulatory impairment. The test is based upon limb elevation which favors drainage of peripheral vessels with subsequent ischemia that releases vasodilating substances. After elevation, the dependent limb position allows filling of the dilated vessels by gravity and the force of the cardiac contraction.

The patient lies flat with his legs elevated to a 90° angle while he flexes and extends his feet repeatedly for one minute. If arterial flow is impaired, the distal portion of the elevated limb exhibits pallor, which may be delayed somewhat when arterial disease is mild. With marked circulatory impairment, pallor may not appear at all since reactive hyperemia may be present before elevation. When the patient sits up and places his legs in a dependent position, reactive hyperemia normally produces a bright red color fairly promptly. A delay of 45 to 60 seconds indicates some degree of arterial impairment.



Flexing and extending legs at 90° angle for one minute.



Sitting up and placing legs in dependent position.

When varicosities are present, this test is not reliable, since skin color may return very promptly in dependency whether arterial circulation is impaired or not.[2] Rapid development of cyanosis in dependency indicates low or absent superficial vessel tone. In continued dependency, intense cyanotic rubor develops slowly when local circulation is impaired.

Awareness of this phenomenon and routine use of this test will undoubtedly further earlier diagnosis, permit institution of therapy sooner, and improve the likelihood of a favorable response to therapy.

(1) Winsor, T.: Peripheral Vascular Diseases, Springfield, Illinois, Charles C Thomas, 1959, pp. 457-458. (2) Abramson, D. I.: S. Clin. North America *40*:3-14 (Feb.) 1960.

VASODILAN IS CLINICALLY EFFECTIVE[1-3]

"In particular, the symptoms of pain, cramping, numbness and cold were consistently relieved."[3]

"Isoxsuprine hydrochloride [VASODILAN] was administered orally for a median period of seven months to 46 patients suffering from arteriosclerosis obliterans. Objective improvement could be demonstrated in 39 (about 85 per cent) of these."[1]

"Isoxsuprine [VASODILAN] was used in the management of arteriosclerosis obliterans in 46 patients...."[2] The average "maximal walking distance, measured in 41 patients, more than doubled...during isoxsuprine [VASODILAN] therapy...."[2]

"With strictly a clinical office approach, isoxsuprine [VASODILAN] was used in the treatment of 100 patients with peripheral vascular disorders. Definite clinical improvement was obtained in 89 per cent of these patients."[3]

VIRTUALLY NO SIDE EFFECTS WITH ORAL DOSAGE[1-3]

In a study of 100 patients, "on an oral dose...no side effects have occurred."[3] "With oral administration, there are no contraindications."[2] "There were no significant side-effects or phenomena suggestive of the existence of contraindications."[1]

Contraindications: There are no known contraindications to oral administration of VASODILAN in recommended doses.

Cautions: VASODILAN should not be given immediately postpartum or in the presence of arterial bleeding. Parenteral administration is not recommended in the presence of hypotension or tachycardia. Intravenous administration is not recommended because of the increased likelihood of side effects.

Side effects: Few side effects occur when given in recommended oral doses. Occasional palpitation and dizziness usually can be controlled by dosage adjustment. Single intramuscular doses of 10 mg. or more may result in hypotension or tachycardia.

Dosage and administration: Oral—10 to 20 mg. (1 to 2 tablets) t.i.d. or q.i.d.; I.M.—5 to 10 mg. b.i.d. or t.i.d. *Supplied:* 10 mg. tablets in bottles of 100; in 2 cc. ampuls containing 10 mg. (5 mg./cc.) for intramuscular use, boxes of 6.

For complete details on indications, dosage, administration, and clinical background of VASODILAN, see the brochure of this product available on request from Mead Johnson Laboratories, Evansville 21, Indiana.

References: (1) Samuels, S. S., and Shaftel, H. E.: J.A.M.A. *171*:142-145 (Sept. 12) 1959. (2) Kaindl, F.; Samuels, S. S.; Selman, D., and Shaftel, H.: Angiology *10*:185-192 (Aug.) 1959. (3) Clarkson, I. S., and Le Pere, D. M.: Angiology *11*:190-192 (June) 1960.

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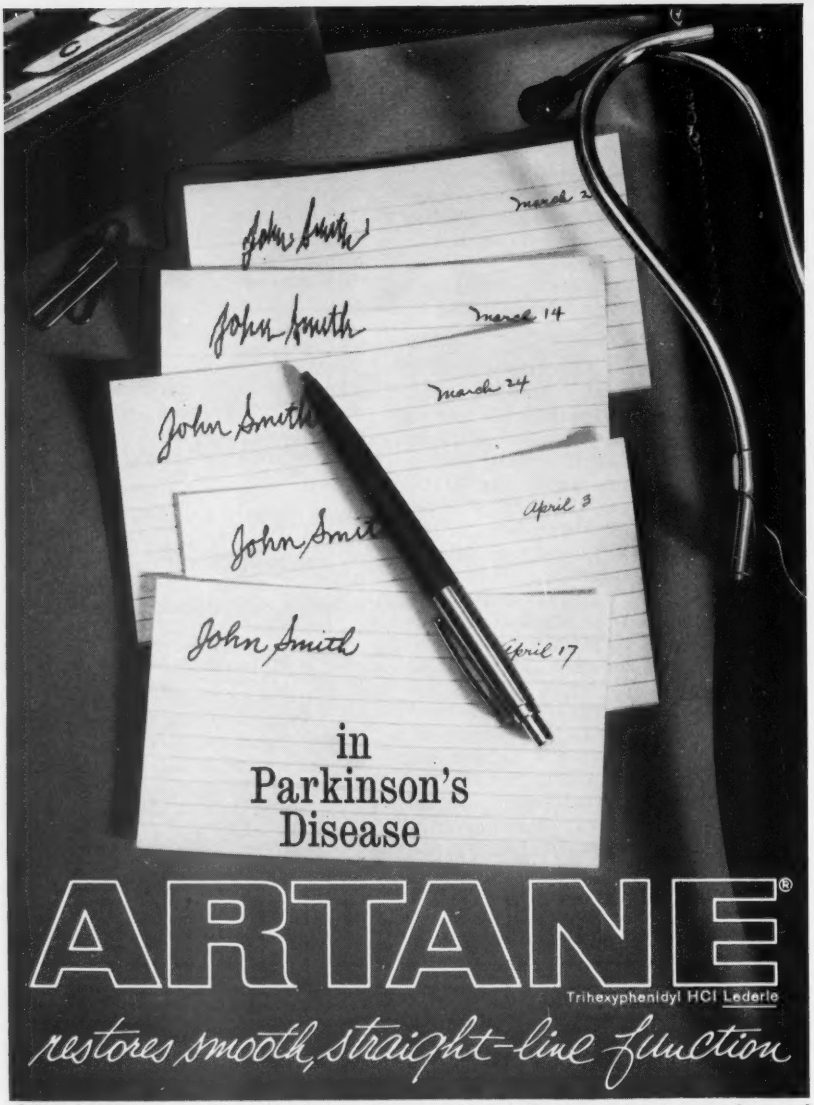

ARTANE is well suited to the needs of the greatest number of patients.[2] Improves rigidity, akinesia and mental depression. Controls oculogyria . . . remarkably free of toxic reactions.[1]

Indicated: All types of Parkinsonism, and to control extrapyramidal reactions in ataractic therapy. Supplied: Tablets, 2 mg. and 5 mg.; Elixir, 2 mg./5 cc. tsp. 1. Constable, K.: J. Am. M. Women's A. 15:757 (Aug.) 1960. 2. Critchley, M.: Brit. M. J. 2:1214 (Nov. 15) 1958.

Request complete information on indications, dosage, precautions and contraindications from your Lederle Representative or write to Medical Advisory Department.

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aspirin buffered with the most widely-prescribed antacid...

in long-term administration, as in Arthritis,
when aspirin combined with an antacid is desired:

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the aspirin buffered with the best

To prevent or minimize gastric distress which often accompanies prolonged or high level administration of acetylsalicylic acid, ASCRIPTIN provides aspirin in combination with MAALOX®, the preferred professional antacid. The recognized superiority of MAALOX makes ASCRIPTIN a superior aspirin-antacid, with the virtues of buffered aspirin and with the added distinction of being promoted professionally only.

Indicated wherever salicylates are useful, ASCRIPTIN is particularly suited to the long-term requirements of your arthritic patients.

Supplied: Bottles of 100 and 500 tablets. For severe pain – Capsules ASCRIPTIN with Codeine (codeine phosphate 15 mg.), bottles of 50.

WILLIAM H. RORER, INC. PHILADELPHIA, PENNSYLVANIA

(Continued from page 66A)

The Conference is to be praised for its regional approach, which could well be emulated throughout the U.S. The physician, however, may find a lack of specific contributions in the medical field a deterrent to a well-rounded volume.

JEROME KAPLAN
Mansfield, Ohio

Chemotherapy in Emotional Disorders

FREDERIC F. FLACH, M.D., and PETER F. REGAN III, M.D., 1960. New York: McGraw-Hill. 282 pages. $10.00.

The current interest in tranquilizing and antidepressant drugs is no doubt accountable for the title of this book; its subtitle, "The Psychotherapeutic Use of Somatic Treatments," would be more apt, for the authors discuss in a concise and easily understood manner all forms of psychiatric therapy. Dynamically oriented psychotherapy is presented as the keystone of treatment.

Psychiatric diagnosis and dynamic factors influencing the choice of proper therapy are presented in the first part of the book. The second part of the volume deals with the effectiveness of the various somatic therapies. The clinical effects of the phenothiazines, reserpine, the barbiturates, meprobamate, stimulants, antidepressant agents, endocrines, electroconvulsive treatment, insulin, and lobotomy are presented in some detail. This section should prove to be of considerable value to all physicians who utilize the above drugs or treatments, since the authors point out how these measures may aid the patient, as well as how they may, in some instances, hinder the progress of therapy.

The third section of the book deals with the integration of treatment methods for the various psychiatric syndromes. The type of psychotherapy to be used and the selection and timing of physical and chemical methods are adequately covered and should aid the physician in caring for his psychiatric patients, as well as in answering the often difficult questions concerning referral of the patient to a psychiatrist or a psychiatric hospital. Of particular interest to the readers of *Geriatrics* is a brief section dealing with the management of patients with organic reactions, including deliria, senile changes, and cerebrovascular disease.

Although recently published, this volume is dated in respect to the antidepressant drugs, since less toxic and more effective compounds have come into use since its publication. The eclectic orientation of the authors does psychiatry great credit and should go far to dispel the myth that psychiatrists are interested either in physical and chemical measures or psychotherapy, for in this brief volume Drs. Flach and Regan have demonstrated that drugs and somatic therapies can be effectively integrated into dynamic psychiatry. Their points of view show sound training, careful reflection, and broad experience and can be well recommended to all physicians interested in improving their skill, comfort, and effectiveness in dealing with patients suffering from emotional disorders.

RICHARD W. ANDERSON, M.D.
Minneapolis

Minds That Came Back

WALTER C. ALVAREZ, M.D., 1961. Philadelphia: J. B. Lippincott. 384 pages. $5.95.

Dr. Alvarez has made a unique and important contribution to the study of the mentally disturbed individual. Those of us who have known Dr. Alvarez have recognized his deep interest in the problems of the emotionally disturbed and the mentally ill. During these years, he has collected biographies of many famous people who were judged insane. There is no question that these people were mentally unbalanced. With his usual brilliant analysis and selection of material, he emphasizes that many of these individuals returned to a normal life. It is also interesting that many persons who are actually insane are able to carry on a normal community life. Dr. Alvarez's many contributions to this field of medicine have reinforced the fact that all practitioners must be aware of the influence

(Continued on page 78A)

"In a controlled clinical study of 260 postcoronary patients, one-half were given sublingual heparin and one-half received conventional treatment. During the period of observation, averaging more than 2 years per patient, there were 12 recurrent infarctions in the heparin-treated group and 38 in the control group. This difference is statistically significant."

Fuller, H. L.: Angiology *11*:200 (June) 1960.

Simple and safe for long-term therapy, Clarin* (sublingual heparin) effectively controls the prolonged postprandial lipemia associated with atherosclerosis by facilitating the normal physiologic breakdown of fats. Unlike parenteral heparin, the use of Clarin requires no clotting-time or prothrombin determinations. The antilipemic activity of each manufactured lot of tablets is confirmed by sublingual control tests in animals.

Indication: For the management of hyperlipemia associated with atherosclerosis, especially in the postcoronary patient. *Dosage:* After each meal, hold one tablet under the tongue until dissolved. *Supplied:* Bottles of 50 pink, sublingual tablets, each containing 1500 I.U. heparin potassium.

An informative booklet, "Hyperlipemia, Heparin and Management of the Postcoronary Patient," is available from Thos. Leeming & Co., Inc., 155 East 44th St., New York 17, N. Y.

*Registered trade mark. Patent applied for.

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✓ from depression to the right frame of mind

✓ continuous, 24-hour cerebral oxygenation for the aging patient. By stimulating respiratory and circulatory function, GERONIAZOL TT* relieves mental confusion, depression, anxiety, and emotional instability—frequent problems in patients after forty—due to presenile changes in the vasculature of the brain. Notable benefit usually is seen within one to three weeks of therapy. It improves appetite, sleep pattern, and outlook—and GERONIAZOL TT* is non-hypertensive, non-excitatory.

Neither a tranquilizer nor a psychic energizer, GERONIAZOL TT* provides a physiologic stimulation of the cerebrum to permit the patient to adjust to his surroundings, become part of life itself again—and *attain the right frame of mind.*

References: 1. Curran, T. R., and Phelps, D. K.: Am. Pract. & Dig. Treat. *11:* 617, 1960. 2. Levy, S.: J.A.M.A. *153:* 1260, 1953. 3. Connolly, R.: W. Va. Med. J. *56:* 263, 1960.

Each TEMPOTROL contains: Pentylenetetrazol, 300 mg.; and Nicotinic Acid, 150 mg.

Indications: Respiratory and circulatory stimulant for the aged and debilitated with symptoms of mental confusion, depression, anxiety or arteriosclerotic psychosis.

Contraindications: None known in recommended dosage.

Dosage: One GERONIAZOL TT* tablet, b. i. d.

Supplied: Bottles of 42 tablets (3 weeks' treatment).

GERONIAZOL® TT*

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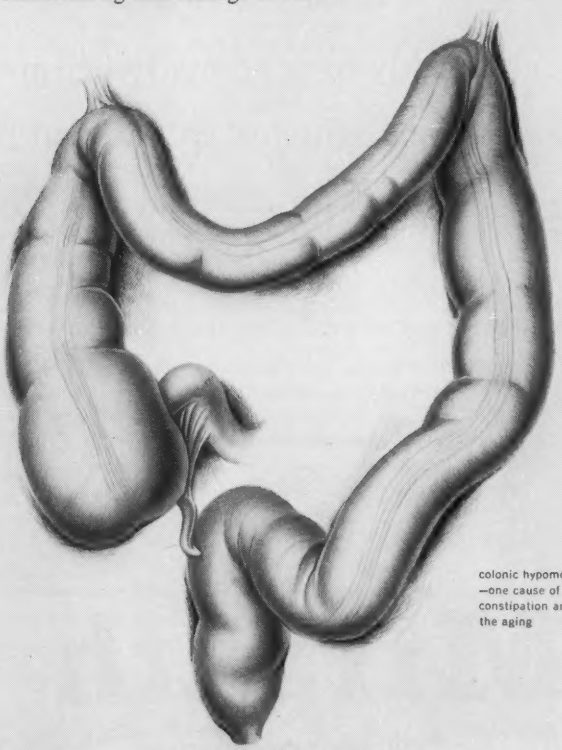

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AVAILABLE IN TWO POTENCIES

MILPATH-400—Yellow, scored tablets of 400 mg. Miltown (meprobamate) and 25 mg. tridihexethyl chloride.
Bottle of 50.

Dosage: 1 tablet t.i.d. at mealtime and 2 at bedtime.

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Dosage: 1 or 2 tablets t.i.d. at mealtime and 2 at bedtime.

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®Miltown + *anticholinergic*

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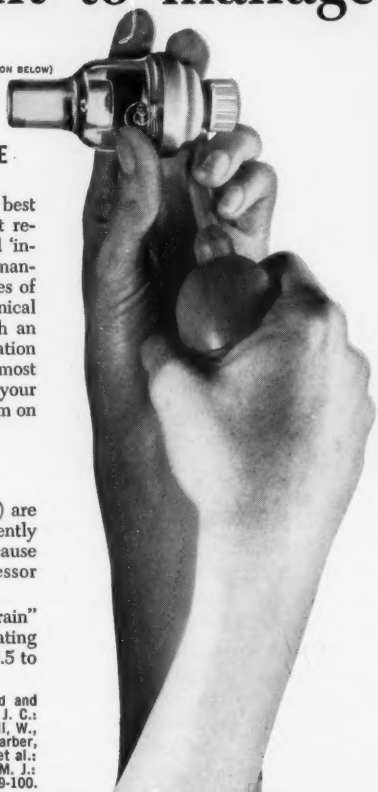
BECAUSE VAPONEFRIN HAS SUCH AN OUTSTANDING RECORD OF SUCCESS WITH INTRACTABLE ASTHMA AND EMPHYSEMA PATIENTS, WE MAKE THIS UNUSUAL OFFER...

Free—a Vaponefrin® Inhalation Set for your difficult-to-manage asthma patient! (USE COUPON BELOW)



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The test of efficacy with any medication can usually be best determined in a difficult case—the case that has not as yet responded satisfactorily to therapy...and is frequently judged 'intractable.' This is why we say, select one of your difficult-to-manage asthma patients to determine the outstanding advantages of Vaponefrin (*racemic* epinephrine). Over 163 published clinical evaluations and standard textbook references* present such an impressive record of success that we offer a Vaponefrin Inhalation Set to your patient *free*—confident that *you* will find it the most effective therapy for continued use. The Set will be sent to your office so that you may present it to the patient and instruct him on its use.

VAPONEFRIN PROVIDES FREE BREATHING IN ASTHMA, EMPHYSEMA AND CHRONIC BRONCHITIS

The clinical advantages of Vaponefrin (*racemic* epinephrine) are abundantly stated in the literature. It can be used confidently even in hypertensive or cardiac patients[1]/is less likely to cause tachycardia than isoproterenol[2]/causes virtually no pressor effects[3]/is far more stable than *l*-epinephrine.[4]

And, unlike many nebulizers which produce an ineffective "rain" of droplets—the Vaponefrin Nebulizer provides a penetrating mist, consistently produces particles in the critical range of 0.5 to 3 microns.[5]

SUPPLIED: Solution, bottles of 7.5, 15 and 30 cc.; Nebulizers, Standard and Pocket size. Also Aerosol Unit. **REFERENCES:** 1. Digilio, V. A., and Munch, J. C.: Ann. Allergy 13:257, 1955. 2. Bickerman, H. A., and Barach, A. L., in Modell, W., Ed.: Drugs of Choice, St. Louis, The C. V. Mosby Co., 1958-59, p. 582. 3. Farber, S. M., and Wilson, R. H. L.: Ann. Int. Med. 50:1241, 1959. 4. Munch, J. C., et al.: J. Am. Pharm. A. (Scient. Ed.) 40:526, 1951. 5. Segal, M. S., and Dulfano, M. J.: Chronic Pulmonary Emphysema, New York, Grune & Stratton, 1953, pp. 99-100. *Bibliography available on request.

The VAPONEFRIN Company • 666 Fifth Ave. • New York 19, N. Y. • Attention: Professional Service Dept. MC
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Patient Identification _____

(Continued from page 72A)

that mental and emotional states have upon the individual's well-being.

The book is well printed and well designed. The material is well selected. It should be in the hands of everyone who in any way is engaged in the care of people. Dr. Alvarez is to be congratulated on what may prove to be the greatest of his many great contributions to medicine.

JOHN F. BRIGGS, M.D.
St. Paul

The Study of Influenza: A Translation from the Russian (Ucheniye o Grippe)

V. M. ZHDANOV, V. D. SOLOV'EV, and F. G. EPSHTEIN, 1960. Washington: U. S. Government Printing Office. PHS Publication No. 792. 939 pages. Illustrated.

Successive epidemics of influenza, including recent waves due to the A-2 (Asian) strain, are characterized by excessive mortality. During such epidemics, the number of deaths is significantly increased among the aged; persons with chronic diseases, especially of the circulatory and respiratory systems; and pregnant women; hence, the current reevaluation of active immunization of these vulnerable population groups.

Timely, therefore, is this translation of a comprehensive monograph by eminent Russian investigators. Vaccine prophylaxis is one of the topics intensively treated. In addition to the review of formolized vaccines and their application, Solov'ev discusses adjuvant vaccines and the live virus vaccine used in the USSR by intranasal installation. Zhdanov gives a detailed presentation of virology, with emphasis upon the variability of influenza viruses and their secular evolution, so important in vaccine composition. Other chapters deal with the history and epidemiology of influenza, immunology, clinical aspects, and laboratory diagnosis. The chapter on treatment by Epshtein and Zhdanov is a rather uncritical description of numerous specific and nonspecific modalities. Some, such as serotherapy by local application, have not been evaluated outside the Soviet sphere.

While not practical as a working manual for the practitioner, *The Study of Influenza* is valuable as an up-to-date review. This function is impaired to some degree for want of an index. An extensive bibliography, with Russian and western references grouped separately, is appended to each of the 10 chapters. The reproduction by photo-offset is quite satisfactory, although some figures lack clarity and occasional typographic errors are noted. The translation is readable.

HAROLD T. FUERST, M.D.
New York City

Basic Psychiatric Concepts in Nursing

CHARLES K. HOFLING, M.D., and MADELENE M. LEININGER, R.N., 1960. Philadelphia: J. B. Lippincott. 503 pages. $6.25.

For a number of years, the nursing profession has been aware of and keenly interested in the dynamics of nurse-patient relationships in psychiatric care.

This text places significant emphasis on 5 psychiatric concepts related to nursing: (1) a comprehensive approach to patient care, (2) patient-centered approach, (3) nurse-patient relationships, (4) dynamic nursing approach, and (5) working together. These concepts help the reader to gain a better understanding of the nurse and her relationships with the patient, his family, representatives of other disciplines, and the people with whom she comes in contact in her daily life.

The authors stress the fact that it is highly important for the nurse to have opportunity to express her feelings. These feelings must be explored and explained in the clinical setting if the nurse is to be effective in the therapeutic milieu.

The differentiation between neurotic and psychotic persons appears in a descriptive, tabular form so that the two kinds of illness can easily be identified. This tabulation should be extremely helpful to nursing students as they work with patients in general and psychiatric hospitals.

(Continued on page 84A)

Quietude for the Hypertensive

As relaxing as a mountain lake...

BUTISERPINE® separates the hypertensive from his anxieties and tensions, lowering the blood pressure conservatively but effectively.

With its gentle calming and hypotensive actions, Butiserpine does not set up a chain of side effects. Its *low* reserpine content (0.1 mg. per tablet) reduces blood pressure smoothly; its 15 mg. of noncumulative BUTISOL SODIUM® butabarbital sodium induces relaxation without depression.

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4 essential actions in one Rx: to bring most hypertensive patients under control

CENTRAL ACTION OF SER-AP-ES:
SER-AP-ES acts centrally to inhibit or block the outflow of sympathetic vasopressor substances. In addition, Ser-Ap-Es improves cerebral vascular tone.

RENAL ACTION OF SER-AP-ES:
Ser-Ap-Es increases renal blood flow, thereby halting or reversing the ischemic process in advancing hypertension. The increase in urine volume and sodium and chloride excretion which occurs with Ser-Ap-Es also benefits the hypertensive patient.

SERPASIL® (reserpine CIBA)
APRESOLINE® hydrochloride (hydralazine hydrochloride CIBA)
ESIDRIX® (hydrochlorothiazide CIBA)

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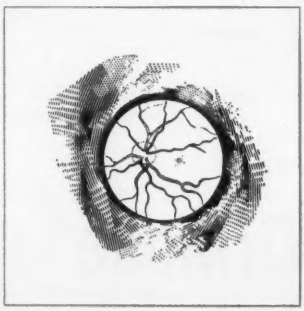
Most hypertensive patients need more than one drug, but most hypertensive patients need only one Rx ... Ser-Ap-Es®



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CARDIAC ACTION OF SER-AP-ES: Ser-Ap-Es has a beneficial effect on the hypertensive heart; diastole is prolonged, and there is a decrease in both heart rate and cardiac output—which combine to ease the strain on the overworked myocardium.

VASCULAR ACTION OF SER-AP-ES: Ser-Ap-Es opposes the action of pressor substances on the vasculature. In addition, Ser-Ap-Es makes the vasculature less responsive to circulating vasopressor amines and more responsive to the antipressor components of the combination tablet.

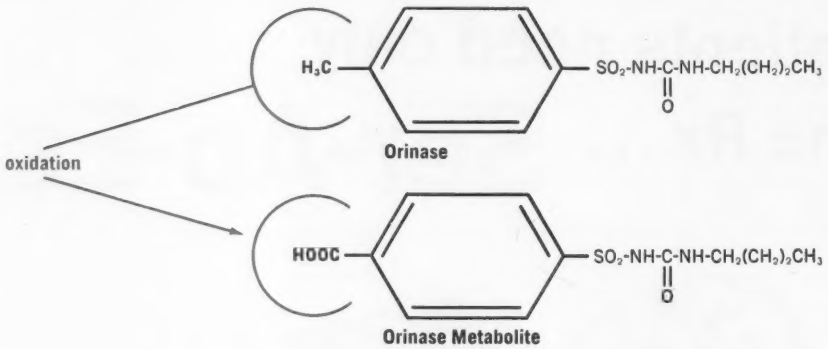
Supplied: SER-AP-ES *Tablets*, each containing 0.1 mg. Serpasil, 25 mg. Apresoline hydrochloride, and 15 mg. Esidrix. *For complete information about Ser-Ap-Es (including dosage, cautions, and side effects), see current Physicians' Desk Reference or write CIBA, Summit, N. J.*

Why is the methyl "governor" in Orinase so important?

One of the most significant advantages of Orinase therapy is the rarity of associated hypoglycemic reactions.

This widely-reported clinical benefit is a function of the exclusive Orinase methyl "governor." Lending itself to ready oxidation (principally, it is thought, a hepatic process), the methyl group ensures prompt metabolic inactivation of the Orinase molecule. What actually happens is that a rapidly- and continuously-excreted carboxy-metabolite is produced that has no hypoglycemic activity at the existing levels.

As a result of the oxidation of its methyl group, Orinase shows a decline in activity soon after it reaches its effective peak in the plasma. Maintenance dosage serves to reduce blood sugar levels to normal, but rarely below that point, and there is no reported problem of accumulation.



Orinase*

An exclusive methyl "governor" minimizes hypoglycemia

Indications and effects: The clinical indication for Orinase is stable diabetes mellitus. Its use brings about the lowering of blood sugar; glycosuria diminishes, and such symptoms as pruritus, polyuria, and polyphagia disappear.

Dosage: There is no fixed regimen for initiating Orinase therapy. A simple and effective method is as follows: *First day*—6 tablets; *second day*—4 tablets; *third day*—2 tablets. The daily dose is then adjusted—raised, lowered or maintained at the two-tablet level, whichever is necessary to maintain optimum control.

Patients receiving insulin (less than 20 units)—discontinue insulin and institute Orinase; (30 to 40 units)—initiate Orinase with a concurrent 30 to 50% reduction in insulin dose with a further careful reduction as response to Orinase is observed; (more than 40 units)—reduce insulin by 20% and initiate Orinase with a further careful reduction in insulin dosage as response to Orinase is observed. In candidates for combined Orinase-insulin therapy, an individualized schedule is usually obtainable during a trial course of two or more weeks.

Contraindications and side effects: Orinase is contraindicated in patients having juvenile or growth-onset, unstable or brittle types of diabetes mellitus; history of diabetic coma, fever, severe trauma or gangrene.

Side effects are mild, transient and limited to approximately 3% of patients. Hypoglycemia and toxic reactions are extremely rare. Hypoglycemia is most likely to occur during the period of transition from insulin to Orinase. Other untoward reactions to Orinase are usually not of a serious nature and consist principally of gastrointestinal disturbances, headache, and variable allergic skin manifestations. The gastrointestinal disturbances (nausea, epigastric fullness, heartburn) and headache appear to be related to the size of the dose, and they frequently disappear when dosage is reduced to maintenance levels or the total daily dose is administered in divided portions after meals. The allergic skin manifestations (pruritus, erythema, and urticarial, morbilliform, or maculopapular eruptions) are transient reactions, which frequently disappear with continued drug administration. However, if the skin reactions persist, Orinase should be discontinued.

Clinical toxicity: Orinase appears to be remarkably free from gross clinical toxicity on the basis of experience accumulated during more than four years of clinical use. Crystalluria or other untoward effects on renal function have not been observed. Long-term studies of hepatic function in humans and experience in over 650,000 diabetics have shown Orinase to be remarkably free of hepatic toxicity. There has been reported only one case of cholestatic jaundice related to Orinase administration, which occurred in a patient with pre-existing liver disease and which rapidly reversed upon discontinuance of the drug.

Each tablet contains:
Tolbutamide ..... 0.5 Gm.

Supplied: In bottles of 50.

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June, 1961

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Book Reviews

(Continued from page 78A)

It is unfortunate that the authors did not include more detail about the behavior of geriatric patients in the chapters on personality development, because this is one of the greatest problems in nursing care. Only a small section of the book is devoted to the process of aging, including a brief description of arteriosclerotic changes.

This excellent book gives a detailed picture of psychiatric nursing concepts and their application in all nursing. Experienced nurses, instructors, students, and members of the interdisciplinary team will find this text useful as they apply this dynamic material in clinical nursing.

JOHN V. GORTON, R.N.
New York

Human Nutrition, Historic and Scientific

IAGO GALDSTON, M.D., editor, 1960. New York: International Universities Press. 321 pages. Illustrated.

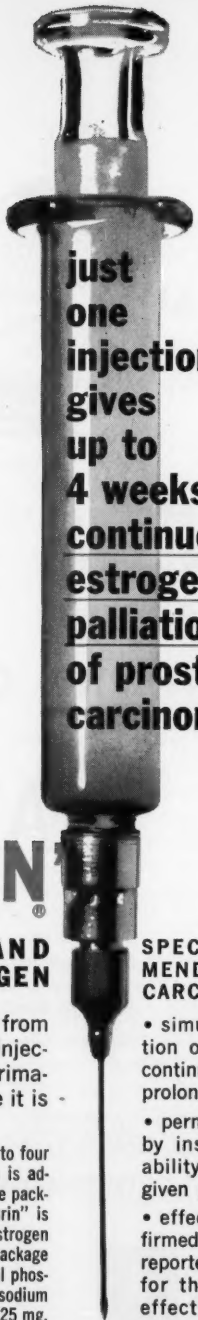
The title of this book is completely descriptive of its contents. Unfortunately, by title, it would appear to be of interest only to a selected number of persons interested in nutrition; actually, material in various chapters has great value for people with a wide variety of interests and occupations. This list would include at least some physicians, biochemists, anthropologists, ecologists, geneticists, and farmers and other persons interested in agriculture, as well as persons who are specifically interested in nutrition.

Material for 20 chapters, with 3 preliminary chapters, is taken from the Third Conference, organized by the Institute on Social and Historic Medicine, New York Academy of Medicine, for a total of 321 pages. There is also an extensive bibliography at the end of most chapters. The subject matter, from a historic past to the present, covers all facets of nutrition on a historic and world-wide basis, as well as specific scientific facts and research programs. Each chapter deals with entirely different subject matter, so that it would be impossible to even attempt to summarize every one, for the facts are multitudinous. The authors are all Ph.D.'s or M.D.'s, with one exception—Henry Wallace, whose chapter on "Development of Improved Crops" by the use of genetics is as interesting as any of the other chapters. Almost all the other authors are professors in various colleges and universities across the United States who teach such subjects as anthropology and sociology, Chinese history, nutrition and biochemistry, public health, ecology, clinical medicine, pediatrics, and biophysics. Some are also directors of foundations, such as the Rockefeller Institute and the Nutrition Foundation. The meat industry is represented by a physician who is the director of laboratories of Swift & Company.

The book can be used as a reference book and needs not be read in its entirety. Food habits in various countries and how they relate to the health of the people, nutrition and population pressures, and other chapters of a historical nature will interest some. Several chapters are of interest to persons concerned with agriculture, livestock and poultry raising, and the dairy industry. Many chapters are of specific interest to physicians. These concern, to list a few, discussions on infant feeding, protein requirements and comparison of mother's milk versus supplementary feeding, the preservation of vitamins by various processing methods and the amounts of specific vitamins saved or supplemented, influence of hormones on metabolic demands, nutritional factors in regulation of fat metabolism, epidemiology of protein malnutritions, nutrition concepts in medicine, and public health; 2 chapters specifically go into research prospective in nutrition. Most of the papers are rather short but all are clearly and concisely written.

If there is any facet of nutrition, historical or current, on an individual, country, or world-wide basis to be researched, then the interested person can undoubtedly

(Continued on page 88A)



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During his convalescence at home, the older patient who continues to receive Sustagen is more likely to hold or increase his nutritional gains. Each glassful you specify adds 390 calories to his diet, including 23.5 Gm. protein, 3.5 Gm. fat, and 66.5 Gm. carbohydrate—plus important quantities of all essential vitamins and minerals.

references

(1) Pareira, M. D., *et al.:* J.A.M.A. *156*:810-816 (Oct. 30) 1954.
(2) Winkelstein, A.: Am. J. Gastroenterol. 27:45-52 (Jan.) 1957.

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(Continued from page 84A)

find some pertinent facts to assuage his interest, with additional bibliographies to assist in his studies.

In the foreword, Dr. Howard Reid Craig, Director of the New York Academy of Medicine, states: "The knowledge acquired during recent decades in respect to the processes of metabolism and the intrinsic factors involved in animal metabolism have, to a great degree, raised our concepts of nutrition from the slough of empiricism to a fairly precise science." In the final chapter, "New Horizons in Research," Charles King, Ph.D., Executive Director, The Nutrition Foundation, Inc., and professor of chemistry, Columbia University, states in his final paragraph, "The integration of basic research in bio-chemistry, genetics, psychology, and broadly in all aspects of the biological sciences is almost certain to build the science of nutrition into an increasingly dominant position in agriculture, medicine, public health, food technology, public education, economics, and even such sciences as population control for the betterment of mankind."

NILA KIRKPATRICK COVALT, M.D.
Winter Park, Florida

The Encyclopedia of Sexual Behavior

ALBERT ELLIS, PH.D., and ALBERT ABARBANEL, PH.D., editors, 1961. New York: Hawthorn Books, Inc. Two volumes. 1,059 pages.

These two large volumes have been well edited. The authors were well chosen, and they have written very well. Everyone who is at all interested in the problems of sex should have a copy of this encyclopedia. Geriatricians will be interested in the article by G. Lombard Kelly on the loss of potency often seen in older men. Interestingly, Lombard Kelly quickly dismisses the possibility of using testosterone, except in those cases in which the man is somewhat eunuchoid or has perhaps lost his testicles because of mumps. As Dr. Kelly so wisely says, even in the older man, much impotence is psychic in origin. Many an older man has lost all interest in his spouse. Sometimes, this is almost entirely her fault, as shown by the fact that her husband can have satisfactory intercourse with a younger and more attractive woman. Dr. Kelly gives many suggestions as to the use of other drugs, some of them sedatives and some of them stimulants. He feels that these drugs can be tried out. He tells also of mechanical devices which can help the man who has a youngish and passionate wife. Lombard Kelly is a great believer in the use of a local anesthetic ointment on the man's glans in the treatment of premature ejaculation.

WALTER C. ALVAREZ, M.D.
Chicago

The Central Nervous System and Behavior

Selected translations from Russian medical literature, 1959. Bethesda, Md.: U. S. Department of Health, Education, and Welfare. 1,051 pages.

This is a group of 70 papers which were translated from the Russian medical literature by the Russian Scientific Translation program of the National Institutes of Health of the United States Public Health Service.

This collection was prepared primarily for critical review by the participants of the Third Macy Conference on the Central Nervous System and Behavior. The articles were selected as being generally representative of some of the more recent Soviet research concerned with the understanding of human behavior. The Russian work is interesting because (1) it represents a sample of more recent developments of a long-standing historical interest in the central nervous system and (2) communication between Soviet scientists and scientists of the Western world has been inadequate.

The result of work in various but related disciplines has been included in this monumental volume. A number of papers are devoted to the early development of conditioned reactions in young children. There is an interesting review of the de-

(Continued on page 96A)

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1. Muir, A., and Cossar: I. A.: Brit. M. J. *2*:7-12 (July 2) 1955. 2. Waterson, A. P.: Brit. M. J. *2*:1531 (Dec. 24) 1955. 3. Brown, R. K., and Mitchell, N.: Gastroenterology *31*:198-203 (August) 1956. 4. Kelly, J. J., Jr.: Am. J. Med. Sci. *232*:119-128 (August) 1956. 5. Brick, I. B.: J. Am. Med. Assn. *163*:1217-1219 (April 6) 1957. 6. Lange, H. F.: Gastroenterology *33*:770-777 and 778-788 (Nov.) 1957. 7. Tebrock, H. E.: Ind. Med. & Surg. *20*:480-482, 1951. 8. Levy, G., Hayes, B. A.: N. Eng. J. Med. *262*:1056 (May 26) 1960. 9. Sleight, P.: The Lancet, p. 305 (Feb. 6) 1960 and p. 932 (April 23) 1960.

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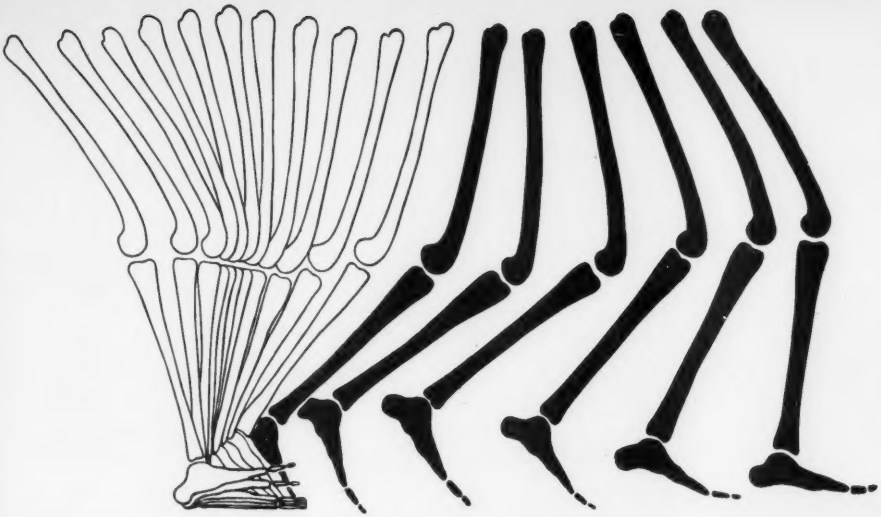

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Relief of pain and swelling was marked or complete in 104 of the 118 (88.1%); duration of response to a single injection was more than three weeks in 89 patients (75.4%) and more than six weeks in 39 of these.[1] "Post-injection flare-up was practically non-existent."[1]

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Precautions

Depo-Medrol for local effect is contraindicated in the presence of acute infectious conditions. Infrequently, atrophic changes in the dermis may form shallow depressions in the skin at the injection site, but these usually disappear in a few months.

Depo-Medrol 40 mg. per cc.
Each cc. contains:

Medrol (methylprednisolone) acetate	40 mg.
Polyethylene glycol 4000	29 mg.
Sodium chloride	8.7 mg.
Myristyl-gamma-picolinium chloride	0.19 mg.
Water for injection	q.s.

Supplied: 1 cc. and 5 cc. vials

20 mg. per cc.
Each cc. contains:

Medrol (methylprednisolone) acetate	20 mg.
Polyethylene glycol 4000	29.6 mg.
Sodium chloride	8.9 mg.
Myristyl-gamma-picolinium chloride	0.19 mg.
Water for injection	q.s.

Supplied: 5 cc. vials

1. Norcross, B. M., and Winter, J. A.: Methylprednisolone acetate: a single preparation suitable for both intra-articular and systemic use, New York J. Med. *61*:552 (Feb. 15) 1961.

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Use Enduron with patients who have mild to moderate hypertension, or patients with edema (as in congestive heart failure, the nephrotic syndrome, hepatic cirrhosis, premenstrual tension, or steroid therapy). Observe its convenience and effectiveness. *We predict you'll be glad you used it.*

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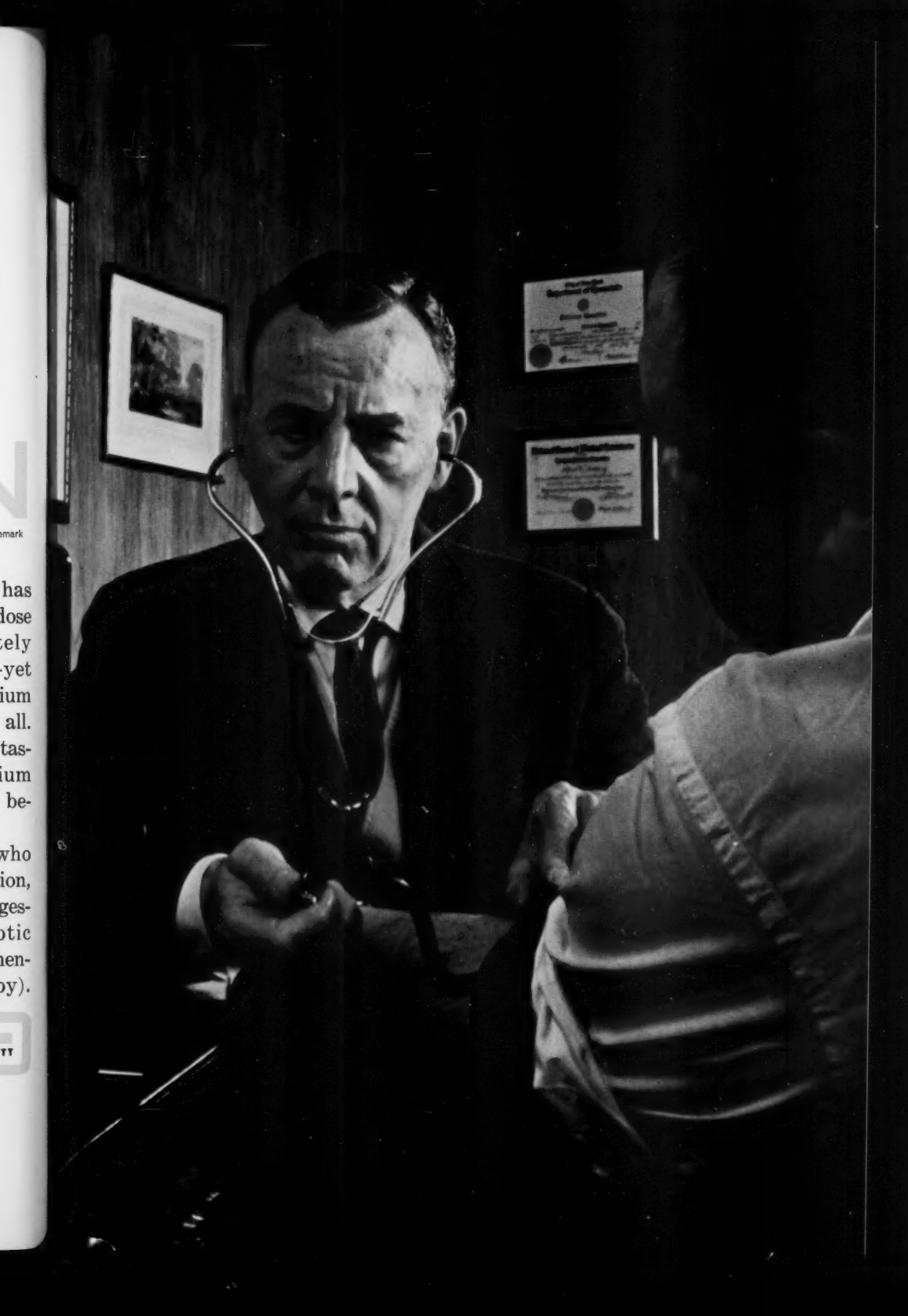

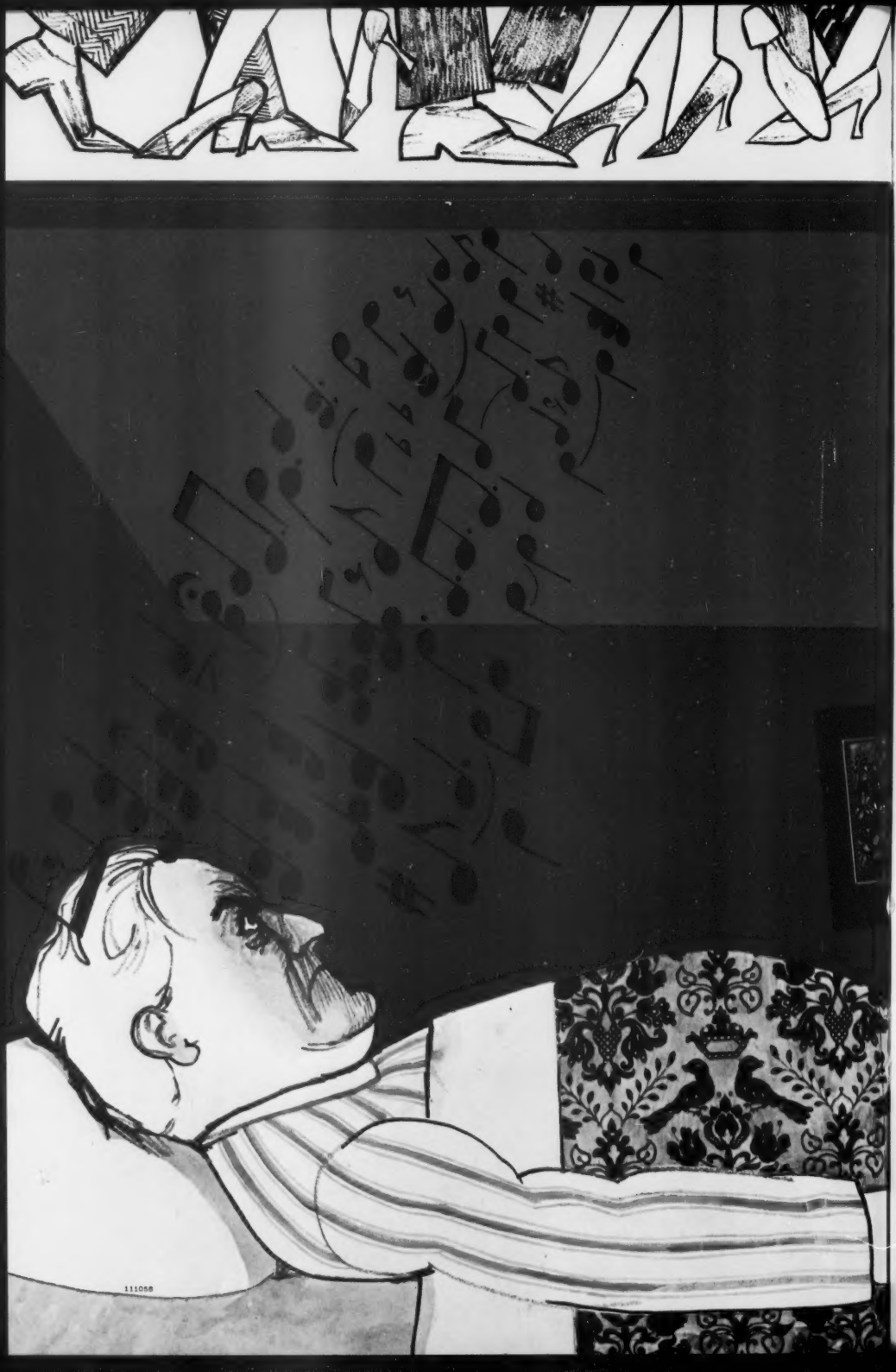

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references: 1. J.A.M.A., 169:41, 1959. 2. J.A.M.A., 173:240, 1960. 3. J.A.M.A., 173:1831, 1960. 4. J.A.M.A., 174:1332, 1960.

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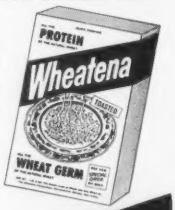

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Book reviews

(Continued from page 88A)

velopment of the theory of reflex activity. A review of the work of the last forty years in embryology in the Soviet Union and in comparative neurology is extremely valuable. The applications of cybernetics to neurology and psychiatry point to some very exciting and promising fields of investigation. These papers also reflect the emphasis placed by Soviet physiologists upon the study of the autonomic nervous system as well as their basic orientation to Pavlovian principles.

This volume is unique in that it allows the interested reader to get an extremely informative and intelligent appreciation of the very important work being conducted in Soviet laboratories. It will undoubtedly prove to be an invaluable source of reference material for investigators in all areas of neurology.

CHARLES M. POSER, M.D.
Kansas City, Kansas

Publications of Geriatric Interest

A Suggested System of Uniform Expense Accounting for Nursing Homes and Related Facilities—proposed expense-accounting system based on findings of studies made of about 100 facilities; stresses need for data on costs of operating these facilities; $1 a copy from Superintendent of Documents, U.S. Government Printing Office, Washington 25, D. C.

Research Highlights in Aging—collection of scientific papers on research in aging; also, literature reviews, training programs, and meetings; free from the Information Officer, Center for Aging Research, National Institutes of Health, Bethesda 14, Maryland.

Activities of the National Institutes of Health in the Field of Gerontology—lists grants for aging research active on January 31, 1961; free from the Information Officer, Center for Aging Research, National Institutes of Health, Bethesda 14, Maryland.

Research Programs in Aging—covers all studies supported or conducted by the National Institutes of Health in the field of

(Continued on page 100A)

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EQUAGESIC not only relieves the arthritic patient's pain and reduces inflammation, but also improves his outlook by controlling the anxiety that magnifies pain. The muscle-relaxant action of EQUAGESIC often allows improved mobility of limbs, thus preventing disabling atrophy and wasting of muscle.

EQUAGESIC will relieve pain, muscle spasm, and tension in a variety of musculoskeletal disorders. Analgesic action is potent, yet non-narcotic. Antianxiety, anti-inflammatory, and muscle-relaxant actions are prompt and reliable.

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Dosage must be individually adjusted until optimal response. Maximum recommended dosage: 800 mg. daily. Supply: Mellaril Tablets, 10 mg., 25 mg., 50 mg., 100 mg.

1. Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959. 2. Judah, L., Murphree, O., and Seager, L.: Am. J. Psychiat. 115:1118, June 1959.

ORIGINAL RESEARCH SERVING THE PHYSICIAN

SANDOZ

Book reviews

(Continued from page 96A)

gerontology; free from the Information Officer, Center for Aging Research, National Institutes of Health, Bethesda 14, Maryland.

Retirement Practices Report of the Saskatchewan Conference on Employment and Retirement of Older Workers—discussions of problems and planning concerning the older worker; write the Aged and Long-term Illness Survey Committee, Regina, Saskatchewan, for more information.

Spanning the Generations—progress report of a project to study human and family relationships and a creative existence for the aged; from Community Services Department, National Council of Jewish Women, 1 West 47th Street, New York 36.

Keep on Living—a guidebook and directory to community resources for the aged in Minnesota; from the Minnesota Department of Public Welfare, Centennial Building, St. Paul 1, Minnesota.

Social Security Rulings on Federal Old-Age, Survivors, and Disability Insurance—includes rulings and decisions, changes in law and regulations, and items of general interest; 25 cents a copy from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D. C.

The Administration of Long Term Care Facilities—$1.50 a copy from The Catholic Hospital Association, 1438 South Grand Boulevard, St. Louis 4, Missouri.

The Changing Problems of the Aged—new concepts of caring for the aged; from the St. Louis Jewish Center for Aged, 1438 East Grand Avenue, St. Louis 7, Missouri.

Training for Friendly Visiting—attitudes in friendly visiting, friendly visiting with blind persons, the friendly visitor in public assistance, and the emotional needs of older persons; 50 cents a copy from the Volunteer Bureau, Welfare Council of Metropolitan Chicago, 123 West Madison Street, Chicago 2.

(Continued on page 102A)

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Product	Calories Per 70 Grams Protein
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1. *Food and Nutrition Board, National Research Council*

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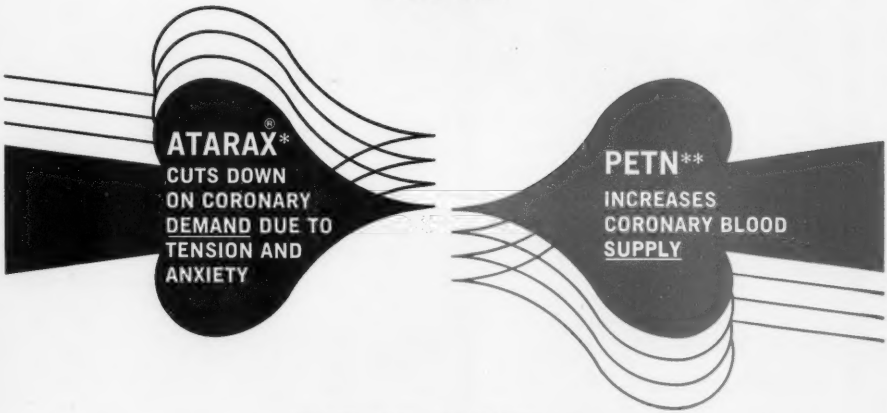

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Give your angina patient better protection by balancing supply and demand...with CARTRAX.

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dosage: Begin with 1 to 2 yellow CARTRAX "10" tablets (10 mg. PETN plus 10 mg. Atarax) 3 to 4 times daily. When indicated, this may be increased by switching to pink CARTRAX "20" tablets (20 mg. PETN plus 10 mg. Atarax). For convenience, write "CARTRAX 10" or "CARTRAX 20."
Supplied in bottles of 100. Prescription only.

1. Clark, T. E., and Jochem, G. G.: Angiology 11:361 (Aug.) 1960.

*brand of hydroxyzine **pentaerythritol tetranitrate

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Science for the World's Well-Being®

Combat Dry Skin Two Ways

Lubriderm, an oil-in-water emulsion for topical application, and Lubath, a bath additive containing cottonseed oil, help overcome the dry, itchy skin generally associated with atopic dermatitis, asteatosis, chapped and chafed skin, wind and sunburn, winter, bath and senile pruritus. Used individually or in combination, Lubriderm and Lubath restore a soft, smooth, comfortable skin condition.

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Highly-refined cottonseed oil made dispersible in hard or soft water by a non-irritating, nonionic surfactant. Effortlessly deposits a thin film of soothing oil over the entire body while bathing.

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61-15R

Book reviews

(Continued from page 100A)

How to Sponsor a Group Program for the Aging—arranging wholesome and worthwhile programs for older groups (Publication No. 8); single free copies from the Health and Welfare Council of the National Capitol Area, 1101 M. Street, N.W., Washington 5, D. C.

New Books Received

Books and publications received will be listed here periodically, and such mention must be regarded as sufficient return for the courtesy of the sender. Books of special interest to our readers will be reviewed as space permits.

American Drug Index, 1961. CHARLES O. WILSON, PH.D., and TONY EVERETT JONES, PH.D., 1961. Philadelphia: J. B. Lippincott. 791 pages. $6.75.

Improving Patient Care Through Education and Regulation. Proceedings of the NATIONAL NURSING HOME INSTITUTE, 1960. Washington, D. C.: American Nursing Home Association. 109 pages. $1.00.

Metabolic Effects of Adrenal Hormones. G. E. W. WOLSTENHOLME, M.A., and MAEVE O'CONNOR, B.S., editors, 1960. Boston: Little, Brown & Co. 109 pages. Illustrated.

Multiple-Choice Examinations in Medicine. JOHN P. HUBBARD, M.D., and WILLIAM V. CLEMANS, PH.D., 1961. Philadelphia: Lea & Febiger. 186 pages. $3.75.

Recent Advances in Renal Disease. M. D. MILNE, editor, 1961. Philadelphia: J. B. Lippincott. 245 pages. Illustrated. $5.00.

Vision of the Aging Patient. MONROE J. HIRSCH and RALPH E. WICK, editors, 1960. Philadelphia: Chilton Co. 297 pages. Illustrated. $7.50.

The Dyslipidoses. RAUL FLEISCHMAJER, M.D., 1960. Springfield, Ill.: Charles C Thomas. 494 pages. Illustrated. $16.00.

Aging in the State of Washington. WILLIAM S. HOPKINS, editor, 1961. Seattle: University of Washington Press. 353 pages. $6.00.

Wisconsin Conference on Work and the Heart. FRANCIS F. ROSENBAUM, M.D., and ELSTON L. BELKNAP, M.D., editors, 1959. New York: Paul B. Hoeber, Inc. 362 pages. Illustrated. $12.00.

Therapeutic Electricity and Ultraviolet Radiation. SIDNEY H. LICHT, M.D., 1959. New Haven, Conn.: Elizabeth Licht, Publisher. 373 pages. Illustrated. $10.00.

Message, Manipulation and Traction. SIDNEY H. LICHT, M.D., editor, 1960. New Haven, Conn.: Elizabeth Licht, Publisher. 258 pages. Illustrated. $10.00.

Fundamentals of Modern Allergy. SAMUEL J. PRIGAL, M.D., editor, 1960. New York: McGraw-Hill Book Co. 671 pages. Illustrated. $18.50.

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This is the promise of Noludar 300... a night of deep, refreshing sleep without risk of habituation or toxicity... 6 to 8 hours of undisturbed rest... an easy awakening in the morning, free of fogginess or barbiturate "hangover." Try Noludar 300 for your next patient with a sleep problem. One capsule at bedtime. Chances are she'll tell you

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patient

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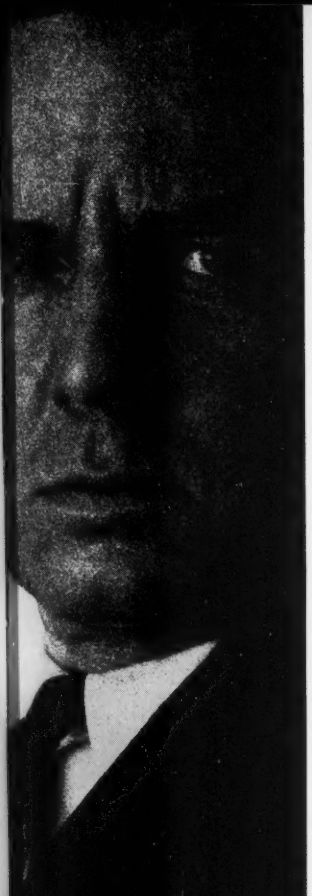
provides remission of depression—smoothly, gradually, without "jarring" □ notably low incidence of serious complications or side effects □ convenience of once-a-day dosage

Science for the world's well-being® Pfizer PFIZER LABORATORIES Division, Chas. Pfizer & Co., Inc. New York 17, New York



restores
the will
to
improve

In Brief Niamid, brand of nialamide, is 1-(2-[benzylcarbamyl] ethyl)-2-isonicotinylhydrazine, a well-tolerated antidepressant that may correct or relieve depression on once-a-day dosage. **Indications:** Depressive syndromes of varying degrees of severity may be responsive to Niamid including: involutional melancholia, postpartum depression, depressed phase of manic-depressive reaction, senile depression, reactive depression, schizophrenic reaction with depressive component, psychoneurotic depression. ■ In neurotic or psychotic patients, Niamid may normalize or favorably modify aberrant or excessive reactions and symptoms of depression such as: phobias, guilt feelings, dejection, feeling of inadequacy, discouragement, worry, uneasiness, distrustfulness, hypochondriacal and nihilistic ideas, difficulty in concentration, insomnia, loss of energy or drive, indecision, hopelessness, helplessness, decreased functional activity, emotional and physical fatigue, irritableness, inability to rest or relax, sadness, anorexia and weight loss, and withdrawal from society. *In the withdrawn patient,* Niamid may elevate the mood so that there is increased activity, increased awareness and interest in surroundings, and increased participation in group activities. Appetite may be increased and there may be decreased fatigability. Lack of clinical response to other antidepressant therapy does not preclude a favorable response to Niamid. Relief of depression may also be evidenced by elimination or reduction of the need for somatic therapy, such as electroshock. *In patients suffering from depression associated with chronic illness,* Niamid may improve mental outlook, reduce the impact of pain, decrease the amounts of narcotics or analgesics needed, and improve appetite and well-being. *In patients with angina pectoris,* Niamid has been found to be a useful adjunct to management through reduction in frequency of attacks and pain. **Dosage:** Starting dosage is 75 to 100 mg. on a once-a-day or divided daily basis. This may subsequently be adjusted depending upon the tolerance and response. Responses to Niamid are not usually rapid, and revisions of dose should be withheld until at least a few days have elapsed at each level. Increments or decrements of 12½-25 mg. are generally sufficient. A daily dosage of 200 mg. is the maximum recommended for routine use. (As much as 450 mg. daily has been used in some patients.) **Side Effects:** Niamid, in clinical use, has been characterized by a significant lack of toxicity. It is generally well tolerated. Nervousness, restlessness, insomnia, hypomania, or mania, sometimes occur. Occasional headache, weakness, lethargy, vertigo, dryness of the mouth, blurred vision, increased perspiration, constipation, mild skin rash, mild leukopenia, and epigastric distress may be obviated or modified by reductions in dose. Effects due to monoamine oxidase inhibition persist for a substantial period following discontinuation of the drug. **Precautions and Contraindications:** Hepatic toxicity has not been reported in extensive clinical studies. However, if previous or concurrent liver disease is suspected, the possibility of hepatic reactions and liver function studies should be considered. ■ The suicidal patient is always in danger, and great care must be exercised to maintain all security precautions. The apathetic patient may obtain sufficient energy to harm himself before his depression has been fully alleviated. ■ Niamid may potentiate sedatives, narcotics, hypnotics, analgesics, muscle relaxants, sympathomimetic agents, thiazide compounds and stimulants, including alcohol. Caution should be exercised when rauwolfia compounds and Niamid are administered simultaneously. Rare instances have been reported of reactions (including atropine-like effects, and muscular rigidity) occurring when imipramine was administered during or shortly after treatment with certain other drugs that inhibit monoamine oxidase. **In Cardiology:** The central effects of Niamid may encourage hyperactivity and the patient should be closely observed for any such manifestation. Orthostatic hypotension or hypertensive episodes occur in a few individuals; cardiac patients should be carefully selected and closely supervised. **In Epilepsy:** Although in some patients therapeutic benefits have been achieved with Niamid, in others the disease has been aggravated. Care should be exercised in the concomitant use of imipramine, since such treatment with monoamine oxidase inhibitors has been reported to aggravate the grand mal seizures. **In Tuberculosis:** Existing data do not indicate whether resistance of M. tuberculosis to isoniazid may be induced with Niamid therapy; nevertheless, it should be withheld in the depressed patient with coexisting tuberculosis who may need isoniazid. ■ As with all therapeutic agents excreted in part via the kidney, due caution in adjusting dosage in patients with impaired renal function should be observed. **Supplied:** Niamid (Nialamide) Tablets, 25 mg.: 100's—pink, scored tablets; 100 mg.: 100's—orange, scored tablets./*More detailed professional information available on request.*

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PART 1

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- A complete compendium of the clinically useful abstracts of current medical literature published in MODERN MEDICINE during the first half of 1961.
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Isordil produces a dramatic decrease in the incidence and severity of Angina Pectoris[1]

- fourteen papers published within the past year document this therapeutic advance.

Isordil "...appears to exert a more consistent and profound effect than any drug previously used for the prophylaxis of angina pectoris."[1] Rapid onset of action and prolonged effect are important advantages over other agents. "Benefits from [Isordil therapy] seemed to be more marked with continued use."[1]

Other studies have shown similar striking results.[2-7] With Isordil, you can expect a "...substantial reduction in frequency and duration of [angina] attacks."[2] Nitroglycerin requirements often can be drastically reduced or eliminated.

why Isordil is different

- With its high solubility, comparable to that of nitroglycerin, Isordil has a much faster onset of action than do some older therapies. For example, with Isordil the therapeutic lag caused by the low solubility of PETN is avoided. Isordil starts to work within 15 to 30 minutes; as fast as two minutes if partially dissolved in the mouth before swallowing.
- Because the liver metabolizes it very slowly, Isordil has a longer duration of action—about 4 to 6 hours.

References: 1. Albert, A.: Isosorbide Dinitrate in Treatment of Angina Pectoris, Journal Lancet 81:112 (Mar.) 1961. 2. Shapiro, S.: Angina Pectoris: Treatment with Isosorbide Dinitrate, Angiology 12:53 (Feb.) 1961. 3. Leslie, R. E.: Coronary Vasodilators—A Comparative Study, Western Medicine 2:56 (Feb.) 1961. 4. Russek, H. I.: Comparative Responses to Various Nitrates in the Treatment of Angina Pectoris, Journal of the Kansas City Southwest Clinical Society 36:14 (Dec.) 1960. 5. Berry, J. W.; Carney, R. and Lankford, H.: Clinical Experiences with Isosorbide Dinitrate (Isordil®), Angiology 12:254 (June) 1961. 6. Sherber, D. A. and Gelb, I. J.: The Clinical Pharmacology of Isosorbide Dinitrate: A Unique, New Nitrated Polyalcohol, **ibid.** 7. Joseph, L. G. and Mancini, A.: Isosorbide Dinitrate in Angina Pectoris, **Ibid.**

Reprints, literature and professional samples available on request. Consult direction circular or Physicians' Desk Reference before prescribing.

FOR ANGINA PECTORIS

Isordil®

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Also Available: ISORDIL WITH PHENOBARBITAL, the accepted sedative for the relief of anxiety in heart patients.

IVES-CAMERON COMPANY, New York 17, N. Y.

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Activities and announcements

All news and announcements for this department should reach the editorial office six weeks before publication date. Please direct all communications to News Editor, GERIATRICS, 84 South Tenth Street, Minneapolis 3, Minnesota.

Future Meetings

The fourteenth annual meeting of the Gerontological Society will be held in Pittsburgh, November 9-11. Each of the 4 professional divisions of the society—clinical medicine, biology, psychology, and social welfare—will have a separate program. A feature of the clinical medicine section will be a day-long colloquium on the pharmacologic principles in the aging patient on Friday, November 10. Society president, Dr. Joseph T. Freeman, will be chairman, with Drs. Stanley R. Mohler, director of the Civil Aeromedical Research Institute in Oklahoma, and Robert H. Dovenmuehle, Center for Aging Research at Duke University, as moderators. Other sessions, such as an educational TV program and a plenary session on cardiopulmonary function in the aging, will be held for the entire membership.

The annual convention of the California Association of Nursing Homes, Sanitariums, Rest Homes and Homes for the Aged will be held in Anaheim, California, November 7-10. At the four-day meeting, representatives of most of the state's privately owned geriatric, convalescent, and mental institutions will discuss the problems of the aged and the ill. Dr. Warren L. Bostick, president of the California Medical Association, will speak. Representatives from neighboring states have also been invited.

Influenza on the Increase

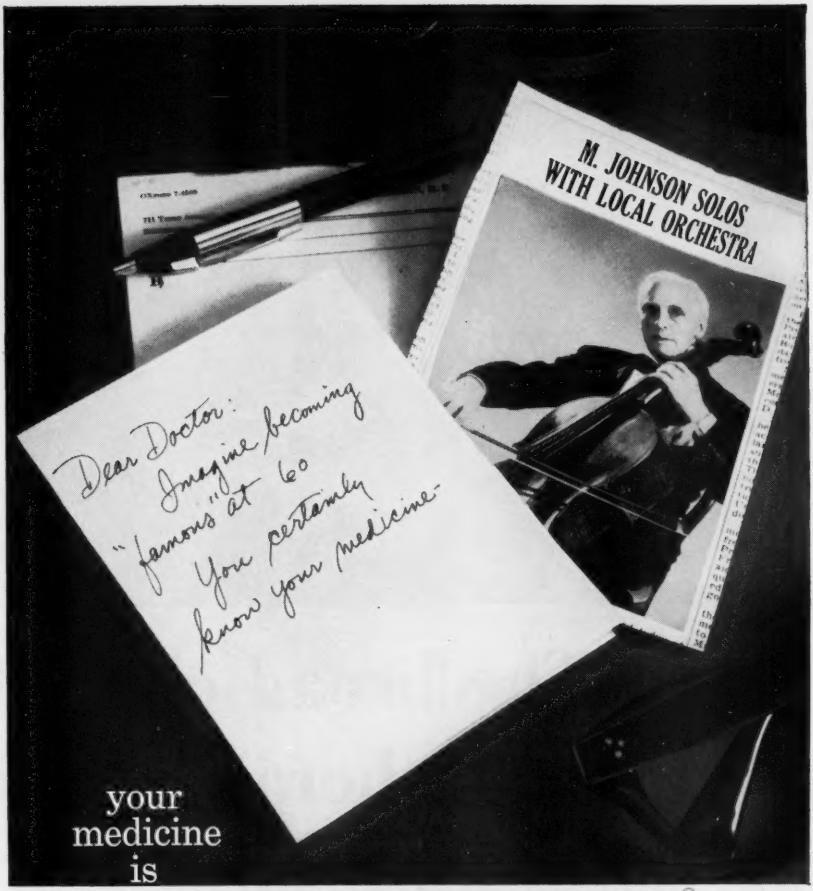
Persons over 65, those with chronic illness, and pregnant women should have influenza shots immediately, says Surgeon General Luther L. Terry of the U.S. Public Health Service. He believes that epidemics are likely this fall and winter, and influenza deaths have occurred most often in these 3 groups. Once flu strikes the community, however, vaccination is useless. Dr. Terry bases his prediction on the usual cycles for influenza—two to three years for the Asian type and four to six years for type B. A recurrence of Asian flu is due about now, and type B is already overdue. Of special significance is the epidemic that struck Europe last year. A similar outbreak in England in 1951 reached the United States in 1952.

Meals on Wheels

The aged, the disabled, and the chronically ill who live in San Francisco can now have meals served to them in their homes at

little cost. The Meals on Wheels project was started last year as a pilot program by the women's auxiliaries of the San Francisco medical and dental societies. Now the

(Continued on page 112A)



GEVRESTIN®

Geriatric Vitamins—Minerals—Hormones—d-Amphetamine Lederle

one capsule every morning supplements the diet to help achieve proper balance: ❖ nutritionally ❖ metabolically ❖ mentally

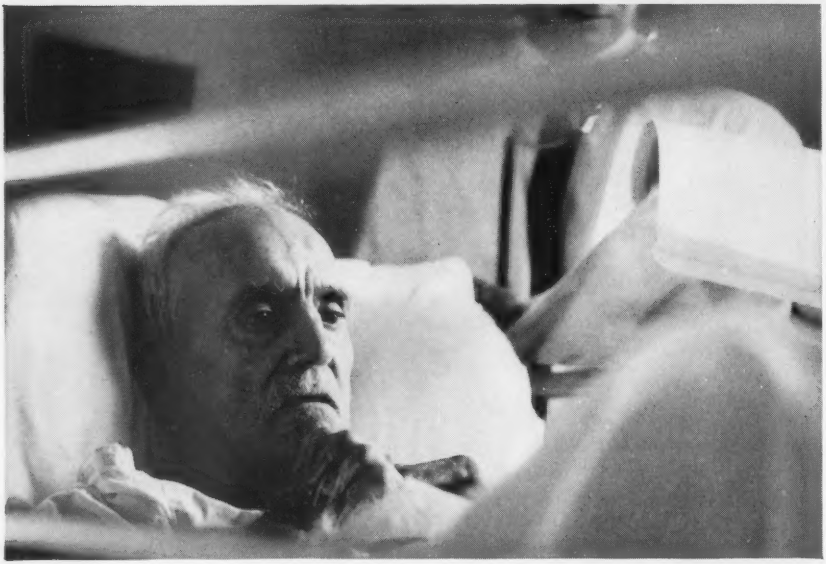
Each dry-filled capsule contains: Ethinyl Estradiol, 0.01 mg. • Methyl Testosterone, 2.5 mg. • d-Amphetamine Sulfate, 2.5 mg. • Vitamin A (Acetate), 5,000 U.S.P. Units • Vitamin D, 500 U.S.P. Units • Vitamin B_{12} with AUTRINIC® Intrinsic Factor Concentrate, 1/15 N.F. Oral Unit • Thiamine Mononitrate (B_1), 5 mg. • Riboflavin (B_2), 5 mg. • Niacinamide, 15 mg. • Pyridoxine HCl (B_6), 0.5 mg. • Calcium Pantothenate, 5 mg. • Choline Bitartrate, 25 mg. • Inositol, 25 mg. • Ascorbic Acid (C) as Calcium Ascorbate, 50 mg. • l-Lysine Monohydrochloride, 25 mg. • Vitamin E (Tocopheryl Acid Succinate), 10 Int. Units • Rutin, 12.5 mg. • Ferrous Fumarate (Elemental iron, 10 mg.), 30.4 mg. • Iodine (as KI), 0.1 mg. • Calcium (as $CaHPO_4$), 35 mg. • Phosphorus (as $CaHPO_4$), 27 mg. • Fluorine (as CaF_2), 0.1 mg. • Copper (as CuO), 1 mg. • Potassium (as K_2SO_4), 5 mg. • Manganese (as MnO_2), 1 mg. • Zinc (as ZnO), 0.5 mg. • Magnesium (MgO), 1 mg. *Supply:* Bottles of 100 and 1,000.

Request complete information on indications, dosage, precautions and contraindications from your Lederle representative or write to Medical Advisory Department.

LEDERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

SEVERE DEBILITY

DURABOLIN improves outlook and appetite, stabilizes protein and mineral metabolism, arrests weight loss, restores strength, vitality.



The broad clinical anabolic therapy with

BEFORE AND AFTER SURGERY

DURABOLIN fortifies the "poor risk" patient, checks nitrogen loss, hastens tissue repair.

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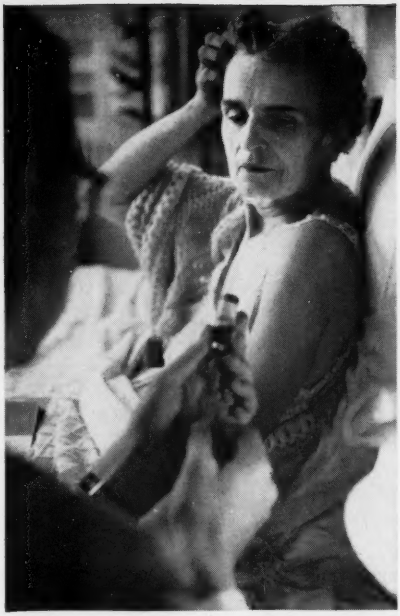
For comprehensive literature, write **Organon Inc., West Orange, N.J.**



INOPERABLE MAMMARY CARCINOMA

In patients responsive to anabolic (androgenic) therapy, DURABOLIN helps reduce pain, improves outlook.

OSTEOPOROSIS

DURABOLIN helps relieve pain, increase mobility through remineralization and reconstruction of the skeletal protein matrix.

usefulness of long-acting Durabolin®

DURABOLIN (nandrolone phenpropionate) is a potent long-acting anabolic stimulant. In many types of illness and injury, DURABOLIN helps speed recovery by reversing catabolic processes, rapidly establishing positive nitrogen balance. A single intramuscular injection weekly or bi-weekly for 12 weeks provides effective anabolic stimulation with little risk of virilizing or hepatotoxic effects. And, because long-acting DURABOLIN is given parenterally, you can be certain your patient has received the correct dose, observe his progress directly.

Dosage: Adults: 50 mg., then 25 to 50 mg., i.m., weekly for twelve weeks. Children: 2-13 years—25 mg., i.m., every 2 to 4 weeks. Infants: half children's dose.

Supplied: DURABOLIN (25 mg./cc.) 5-cc. vials, 1-cc. ampuls (box of 3). DURABOLIN-50 (50 mg./cc.) 2-cc. vials.

UNDERWEIGHT CHILDREN

DURABOLIN helps increase appetite, strength and vitality, stimulates gains in solid, muscular weight and height.

throughout
the
entire
G. I.
tract–
throughout
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entire
pH
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active

gustase™

tri-enzymatic digestion
of carbohydrates, proteins,
vegetable roughage (cellulose)

As indicated in: dyspepsia, colitis, flatulence, constipation, diverticulitis, abdominal distention.

Each tablet contains: Gerilase (standardized amylolytic enzyme) 30 mg., Geriprotase (standardized proteolytic enzyme) 6 mg., Gericellulase (standardized cellulolytic enzyme) 2 mg.

GERIATRIC PHARMACEUTICAL CORP.
45 Commonwealth Blvd., Bellerose, New York

Announcements

(Continued from page 108A)

Pi Beta Phi Alumnae Club is also participating, and the project is a permanent one.

As in other cities where Meals on Wheels is in operation (*Geriatrics* 16: 237, 1961), recipients are selected because they are unable to prepare their own meals and have no one to cook for them. Meals are prepared by a part-time paid cook, the project's only paid employee, in the kitchen of the San Francisco Medical Society Building and are delivered by members of the parent organizations in their own cars. The program is licensed and inspected by the San Francisco Health Department, and menus are planned by a volunteer dietitian.

Dr. Jolliffe Dies

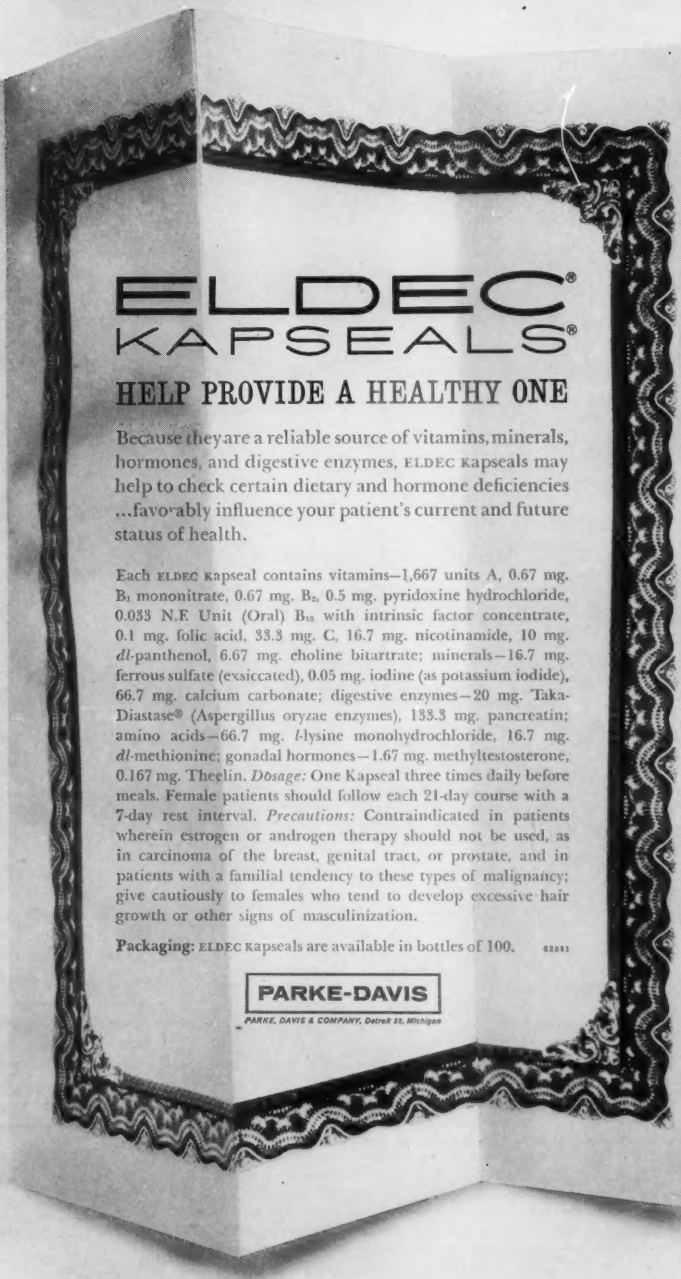
Dr. Norman Jolliffe, 60, director of the New York City Department of Health's bureau of nutrition and an associate editor of *Geriatrics,* died August 1 in New York. A past president of the National Vitamin Foundation and diplomate of the American Board of Internal Medicine and the American Board of Preventive Medicine, Dr. Jolliffe directed nutrition surveys in the United States and in foreign countries. He created the first nutrition clinic in New York City in 1945 and was a pioneer in the theory that a reduction in blood cholesterol levels can reduce incidence of coronary heart disease.

Lack of Respect for Adults

Disrespect for aged persons and juvenile delinquency are both part of the same trend in our society, believes Maurice Linden, director of the Division of Mental Health of the Philadelphia Department of Public Health. Emphasis on youth and the needs of youth, he says, has led to a decline in the importance of the older person and at the same time has contributed to the rise in juvenile delinquency by giving the young person an exaggerated idea of his own importance. Dr. Linden suggests that old per-

(Continued on page 116A)

A RETIREMENT FUND HELPS PROVIDE A SECURE FUTURE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HELP PROVIDE A HEALTHY ONE
Because they are a reliable source of vitamins, minerals, hormones, and digestive enzymes, ELDEC Kapseals may help to check certain dietary and hormone deficiencies ...favorably influence your patient's current and future status of health.
Each ELDEC Kapseal contains vitamins—1,667 units A, 0.67 mg. B_1 mononitrate, 0.67 mg. B_2, 0.5 mg. pyridoxine hydrochloride, 0.033 N.F. Unit (Oral) B_{12} with intrinsic factor concentrate, 0.1 mg. folic acid, 33.3 mg. C, 16.7 mg. nicotinamide, 10 mg. *dl*-panthenol, 6.67 mg. choline bitartrate; minerals—16.7 mg. ferrous sulfate (exsiccated), 0.05 mg. iodine (as potassium iodide), 66.7 mg. calcium carbonate; digestive enzymes—20 mg. Taka-Diastase® (Aspergillus oryzae enzymes), 133.3 mg. pancreatin; amino acids—66.7 mg. *l*-lysine monohydrochloride, 16.7 mg. *dl*-methionine; gonadal hormones—1.67 mg. methyltestosterone, 0.167 mg. Theelin. *Dosage:* One Kapseal three times daily before meals. Female patients should follow each 21-day course with a 7-day rest interval. *Precautions:* Contraindicated in patients wherein estrogen or androgen therapy should not be used, as in carcinoma of the breast, genital tract, or prostate, and in patients with a familial tendency to these types of malignancy; give cautiously to females who tend to develop excessive hair growth or other signs of masculinization.
Packaging: ELDEC Kapseals are available in bottles of 100. 62611
PARKE-DAVIS
PARKE, DAVIS & COMPANY, Detroit 32, Michigan

High-concentration topical salicylate-menthol therapy (BEN-GAY) offers safe, penetrating relief of painful joints and muscles resulting from overexertion.

New, objective evidence:

A double-blind study[1] has reaffirmed the exceptional efficacy and safety of conservative, local treatment of chronic rheumatic disorders with BEN-GAY® (BAUME BENGUÉ), a high-concentration salicylate-menthol compound.

The local and systemic effects of BEN-GAY were evaluated by entirely objective methods in 211 subjects of both sexes suffering from various types of chronic arthritis, bursitis, neuralgia, myalgia and lumbago. Changes in range of joint motion were determined by goniometer and by flexion. Topical application of BEN-GAY measurably improved articular function in 94% when physical therapy was also used, and in 61% without adjunctive treatment. Efficient absorption of salicylate through the skin was indicated by an average urinary excretion of 15 mg. in 24 hours. No ill effects were reported or observed.

Benefits of Topical Salicylate

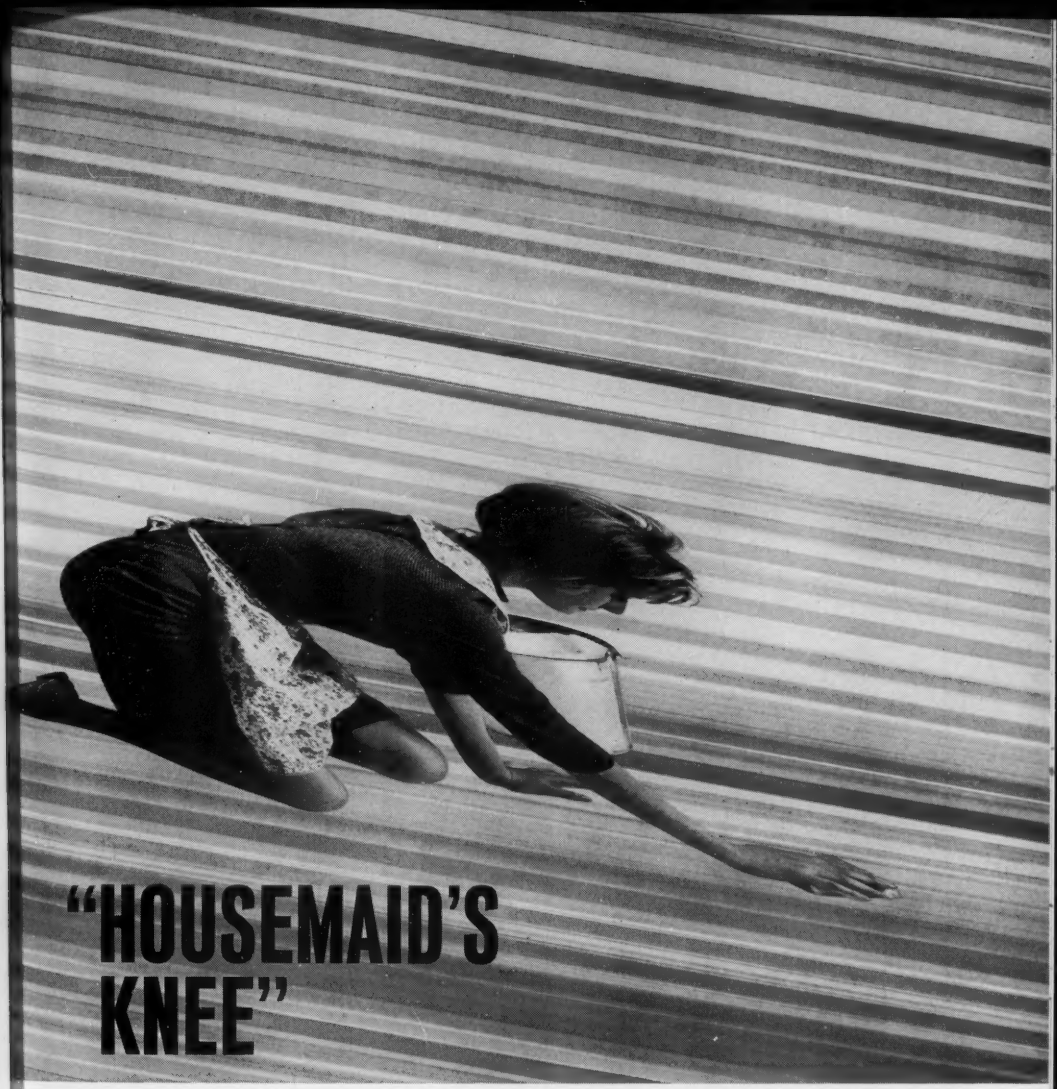
in chronic rheumatic disease

Menthol-induced hyperemia plus high local concentration of salicylate has been recently rediscovered as one of the safest and most promptly effective remedies for rheumatoid discomfort due to exposure.

This controlled study offers new evidence of the efficacy and safety of local treatment of chronic rheumatic disease with BEN-GAY, one of the safest and most reliable formulae at the physician's disposal. BEN-GAY is available in two strengths, *Regular and Children's*. THOS. LEEMING & CO., INC., 155 East 44th St., New York 17, N.Y.

[1]Brusch, C.A., et al.: Md. State Med. J.; 5:36, 1956.

***More efficient salicylate penetration* of treated area and quicker relief of pain is now made possible by the water-washable GREASELESS-STAINLESS BEN-GAY.**



"HOUSEMAID'S KNEE"

...and other painful or disabling musculoskeletal conditions often respond rapidly to the "antidoloritic"* effects of DECAGESIC. DECAGESIC helps restore normal function by relieving pain and discomfort, suppressing inflammation...and often adds a sense of well-being and renewed strength. DECAGESIC combines the benefits of DECADRON® and aspirin with aluminum hydroxide to provide increased efficacy with a lower incidence of side effects.

Decagesic®

dexamethasone with aspirin and aluminum hydroxide

FOR CONSERVATIVE MANAGEMENT OF MUSCULOSKELETAL SYNDROMES

Indications: Mild to moderate inflammatory, rheumatic and musculoskeletal disorders, and conditions in which the conjunctive use of steroid and salicylate is indicated.

Dosage: 1 or 2 tablets 3 or 4 times daily. The usual precautions of corticosteroid therapy should be observed. Before prescribing or administering DECAGESIC, the physician should consult the detailed information on use accompanying the package or available on request.

Supplied: Bottles of 100. Each tablet contains 0.25 mg. of DECADRON dexamethasone, 500 mg. of aspirin (acetylsalicylic acid) and 75 mg. of aluminum hydroxide (present as the dried gel).

*The term "antidoloritic" has been coined by Merck Sharp & Dohme to describe an agent designed to allay pain associated with inflammation—dolor = pain, itic = associated with inflammation.

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MERCK SHARP & DOHME • Division of Merck & Co., Inc., West Point, Pa.

Announcements

(Continued from page 112A)

sons play a larger and more affirmative role with young people, within both the family and the community, by active participation in volunteer work with community youth groups and social agencies.

Home Care Tested

A planned program of therapy in the home, under the supervision of the patient's physician, is being tested by New Jersey Blue Cross and 4 New Jersey hospitals. The experimental home care program is to determine whether Blue Cross subscribers occupying beds in voluntary general hospitals might be placed on home care if such services were available to the public. The plan includes arrangements for some hospital services, coordinated with existing community facilities, to be given in the home with reimbursement to the hospital, by Blue Cross.

Longevity Trends

Iowa has the highest percentage—11.9 per cent of total population—of residents 65 years of age and over, according to an advance report of the 1960 Census of Population. Missouri ranks second, with 11.7 per cent, and Nebraska is third, with 11.6 per cent. Florida, New Hampshire, and Vermont are tied for fourth place, with 11.2 per cent. The 2 newest states, Alaska and Hawaii, have only 2.4 and 4.6 per cent, respectively, in the 65-and-over age category.

Elderly Work Part-time

The New Jersey Highway Authority has a program in which men over 65 are hired to work as part-time toll collectors on the Garden State Parkway. The program was arranged with the State Division of the Aging. Katherine E. White, authority chairman, says the program recognizes the ability, as well as the availability, of the over-65 age group for part-time work.

IN PROBLEM CASES OF
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ESPECIALLY IN THE ELDERLY

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SAFE FOR PROLONGED USE
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Urolitia is bacteriostatic, non-toxic, does not produce drug-fastness, provides simple dosage, and is economical for long term therapy.

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Urolitia is especially useful for elderly patients with residual urine due to cystocele or enlarged prostate, in whom permanent sterilization of the urine cannot be expected.

Urolitia—each tablespoonful contains:

Methenamine	20 gr.
Lithium Benzoate	5 gr.
Sodium Benzoate	2 gr.

In a soothing demulcent menstruum of Triticum and Zea.

DOSE: 1 tbs. in ½ cup warm water ½ hr. a.c. and h.s.
Decrease dose after second day.
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Capillary damage – increased permeability – is a uniform basic reaction resulting from injury or stressors of various types:

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The multiple activities of the citrus bioflavonoids in the prevention or reversal of the inflammatory process include: (1) Maintenance of capillary integrity, (2) In cellular metabolic processes, by potentiating corticosteroids, vitamins and essential nutrients, and by inhibition of hyaluronidase, and (3) Direct anti-inflammatory action.

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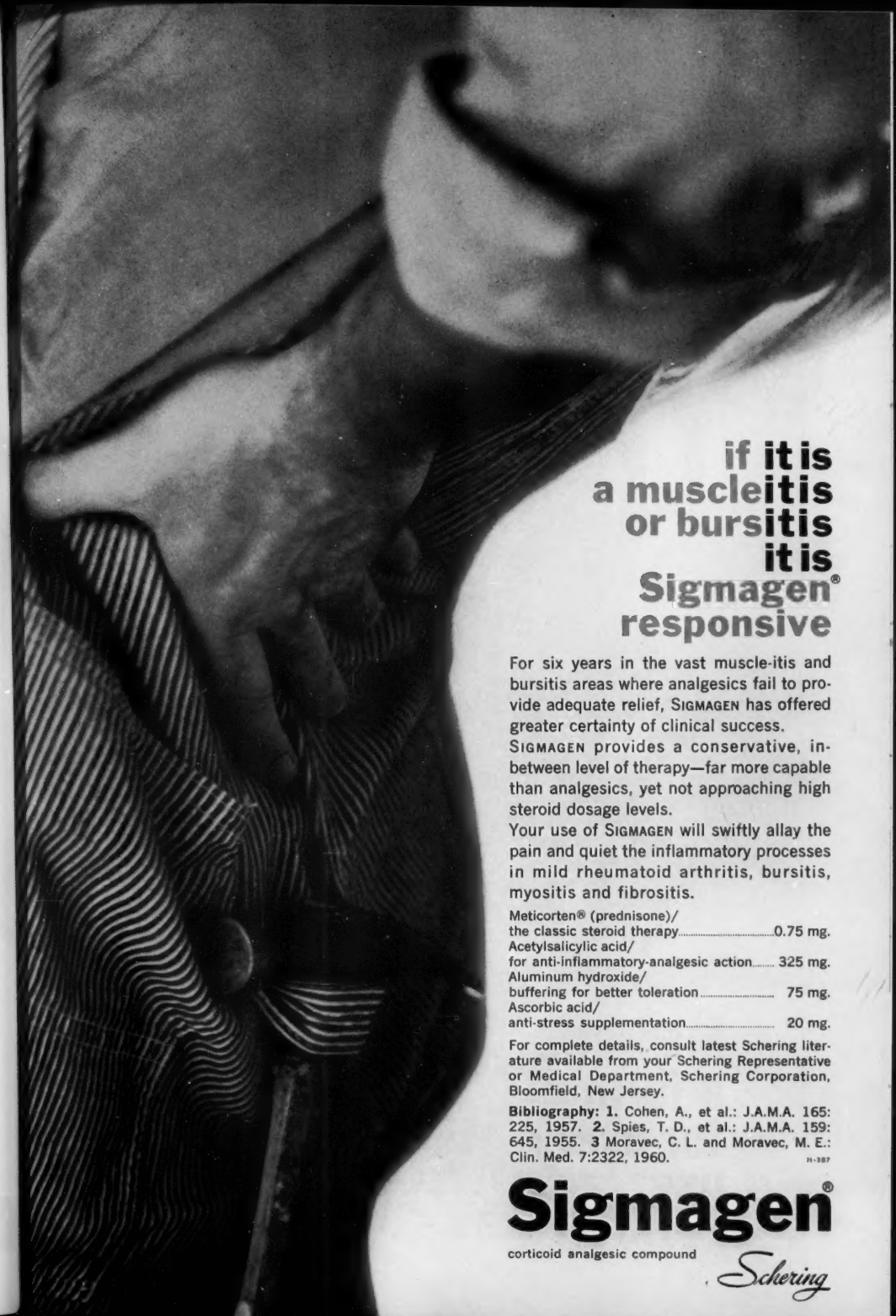

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Bibliography: 1. Cohen, A., et al.: J.A.M.A. 165: 225, 1957. 2. Spies, T. D., et al.: J.A.M.A. 159: 645, 1955. 3 Moravec, C. L. and Moravec, M. E.: Clin. Med. 7:2322, 1960.

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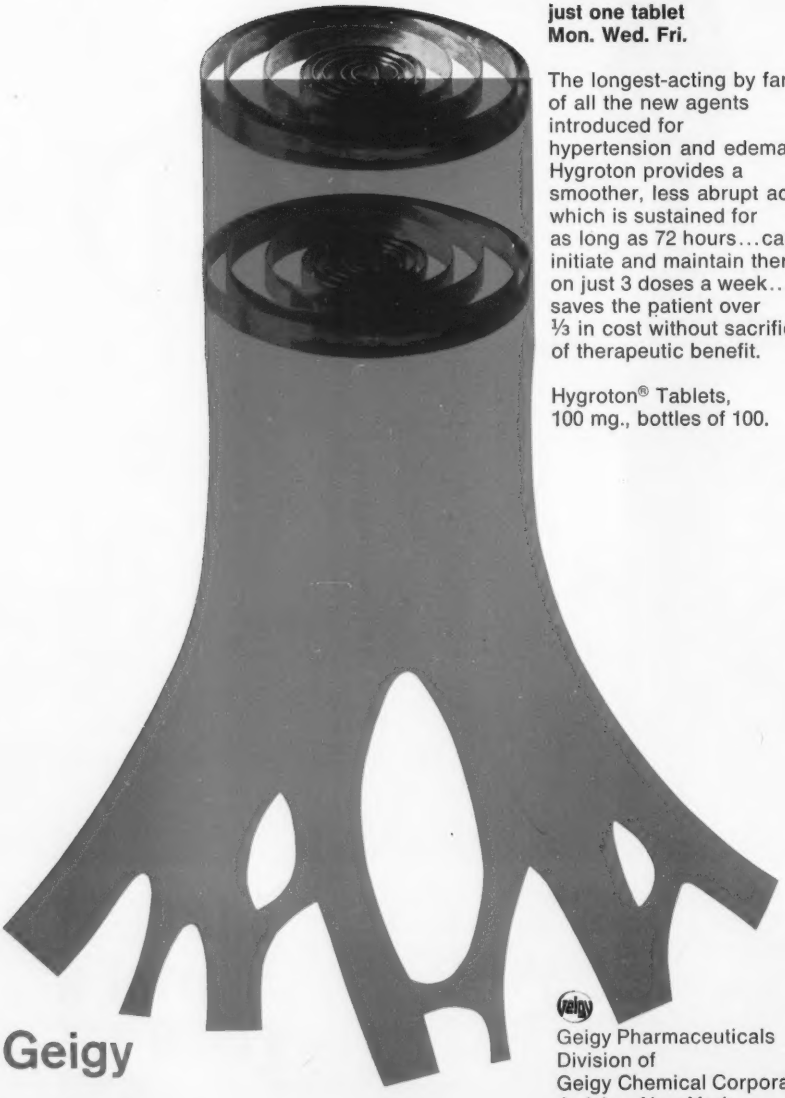

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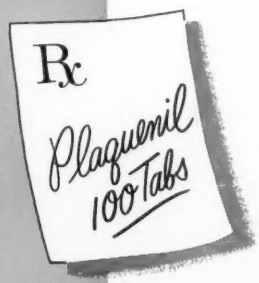

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